```
=> fil reg
FILE 'REGISTRY' ENTERED AT 17:40:52 ON 04 MAR 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     3 MAR 2003  HIGHEST RN 496834-05-0
DICTIONARY FILE UPDATES:    3 MAR 2003  HIGHEST RN 496834-05-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available.  See HELP
PROPERTIES for more information.  See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d sta que l17
L1                STR
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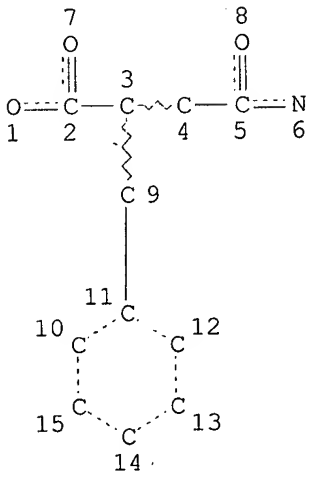

Jan Delaval
Reference Librarian
Biotechnology & Chemical Library
CM1 1E07 – 703-308-4498
jan.delaval@uspto.gov

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NODE ATTRIBUTES:
NSPEC   IS R      AT   6
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  15

STEREO ATTRIBUTES: NONE
L3                STR
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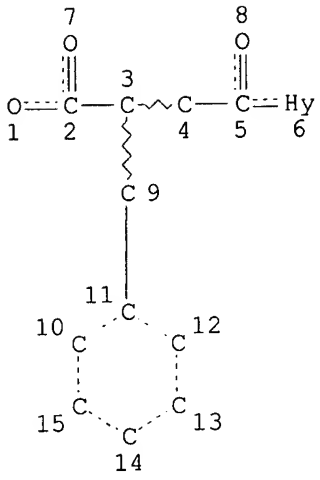

NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS PCY AT 6
DEFAULT ECLEVEL IS LIMITED
ECOUNT IS M1 N AT 6

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE
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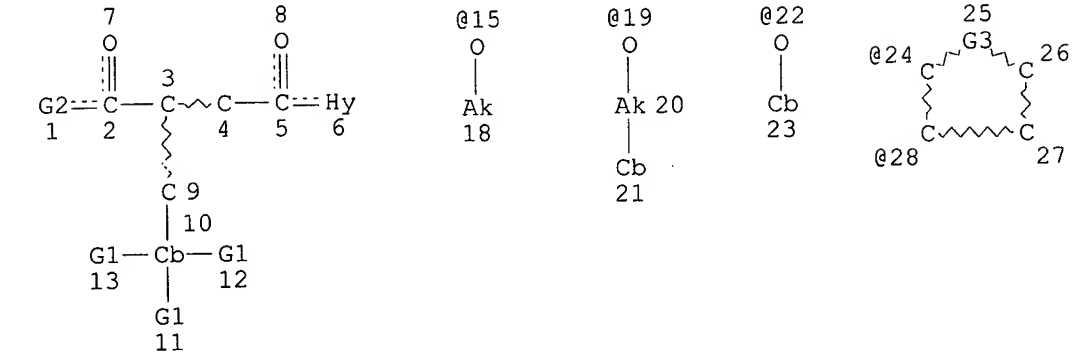
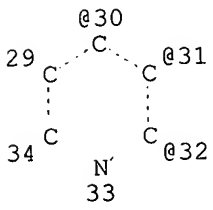
L6 423 SEA FILE=REGISTRY SUB=L5 SSS FUL L3
L9 STR





VAR G1=H/X/AK/15/24/28/30/31/32/CB
VAR G2=OH/15/19/22
VAR G3=O/S
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM

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GGCAT   IS PCY  AT   6
GGCAT   IS MCY  UNS  AT  10
DEFAULT ECLEVEL IS LIMITED
ECOUNT  IS M1 N  AT   6

GRAPH ATTRIBUTES:
RSPEC  24  29
NUMBER OF NODES IS  31

STEREO ATTRIBUTES: NONE
L11          164 SEA FILE=REGISTRY SUB=L6 CSS FUL L9
L12          133 SEA FILE=REGISTRY ABB=ON  PLU=ON  L11 AND 1/NC
L13           15 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND (NC4-C6-C6 OR
                 NC4-OC4 OR NC4-SC4)/ES
L14           10 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 AND (OXIREN? OR DIOX? OR
                 EPOX?)
L15          108 SEA FILE=REGISTRY ABB=ON  PLU=ON  L12 NOT (L13 OR L14)
L16            9 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 AND METHANO?
L17           99 SEA FILE=REGISTRY ABB=ON  PLU=ON  L15 NOT L16


=> d his l17-

     (FILE 'REGISTRY' ENTERED AT 17:07:38 ON 04 MAR 2003)
L17           99 S L15 NOT L16
L18           21 S L17 AND SPIRO
L19           78 S L17 NOT L18

     FILE 'HCAPLUS' ENTERED AT 17:23:39 ON 04 MAR 2003
L20           34 S L19
L21            1 S L18
L22           35 S L20,L21
                 E CAILLE D/AU
L23           21 S E3,E5
L24         3679 S (SANOFI? OR SYNTHELABO?)/PA,CS
L25            2 S L22 AND L23,L24
L26       187625 S ?ARTHRIT? OR ?INFLAM?
                 E ARTHRITIS/CT
L27        11734 S E3-E25
                 E E3+ALL
L28        20616 S E6+NT
                 E E19+ALL
L29         4559 S E5,E4+NT
                 E INFLAMMATION/CT
L30        48599 S E3-E24
                 E E3+ALL
L31        75108 S E2+NT
L32        15998 S E35+NT OR E37+NT OR E38+NT
                 E E36+ALL
L33        48702 S  E4,E5,E3+NT
L34            2 S L22 AND L26-L33
L35            3 S L25,L34
L36           28 S L22 AND (?DIABET? OR ?RETINOPATH?)
L37            3 S L22 AND (?DIABET? AND ?RETINOPATH?)
                 E RETINOPATHY/CT
                 E E3+ALL
L38         2626 S E2
                 E DIABETIC RETINOPATHY/CT
                 E E3+ALL
L39         1524 S E2
L40            2 S L22 AND L38,L39
L41            5 S L35,L37,L40
                 E LUMBAGO/CT
```

```
L42            0 S L22 AND LUMBAGO
L43            0 S L22 AND PAIN?
L44            0 S L22 AND ?TRAUMA?
L45            2 S L22 AND ANALGES?
                 E ANTIPYRETIC/CT
L46            1 S L22 AND E8,E9
                 E 8+ALL
                 E ANTIPYRETIC/CT
                 E E8+ALL
L47            1 S L22 AND E3+NT
                 E E11+ALL
L48            0 S L22 AND E3,E2+NT
L49            0 S L22 AND (FEVER? OR HYPERTHERM? OR HYPERPYREX? OR PYREX?)
L50            5 S L41,L45,L46,L47
L51           18 S (L19 OR L18)(L)THU/RL
L52           13 S L51 NOT L50
L53            2 S L22 AND (ENT OR EYE OR NOSE OR ?NASAL? OR THROAT)
L54            5 S L50,L53
L55           28 S L22 AND P/DT
L56           23 S L22 AND (PD<=20000509 OR PRD<=20000509 OR AD<=20000509)
L57            2 S L56 AND L54
L58           19 S L56 AND L55
L59            3 S L54 NOT L57
L60           17 S L58 AND L26-L54
                 SEL DN AN 1-3
L61           14 S L60 NOT E1-E9
L62            6 S L56 NOT L57,L60
L63            1 S L62 AND (1 OR 63)/SC,SX
L64            2 S L62 AND ?DIABET?
L65           16 S L57,L61,L63,L64
L66           16 S L25,L65
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 17:37:31 ON 04 MAR 2003
L67           91 S E10-E100
L68            1 S 145375-43-5
L69           25 S C19H25NO3 AND L5
L70           10 S L69 AND 1/NC
L71            6 S L70 AND L6
L72            4 S L71 AND  ISOINDOL?

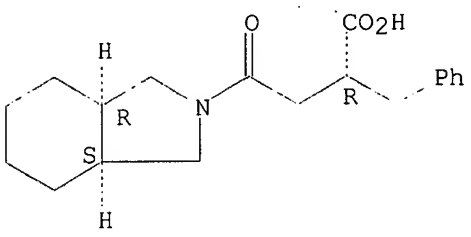
     FILE 'HCAPLUS' ENTERED AT 17:39:54 ON 04 MAR 2003
L73           27 S L68 OR L72
L74           16 S L73 AND L56
L75           12 S L74 AND P/DT
L76            1 S L74 AND L26-L33,L38-L39,L45-L47

     FILE 'REGISTRY' ENTERED AT 17:40:52 ON 04 MAR 2003

=> d ide can tot l72

L72  ANSWER 1 OF 4  REGISTRY  COPYRIGHT 2003 ACS
RN   145375-44-6  REGISTRY
CN   2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-
     (phenylmethyl)-, (.alpha.R,3aR,7aS)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-
     (phenylmethyl)-, [2(R)-cis]-
FS   STEREOSEARCH
MF   C19 H25 N O3
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
```

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

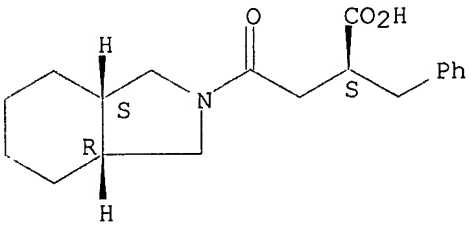
2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 129:27913

REFERENCE 2: 118:59584

L72 ANSWER 2 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 145375-43-5 REGISTRY
CN **2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, [2(S)-cis]-**
OTHER NAMES:
CN Mitiglinide
FS STEREOSEARCH
MF **C19 H25 N O3**
CI COM
SR CA
LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CIN, DRUGPAT, DRUGUPDATES, EMBASE, MEDLINE, PROMT, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

26 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
27 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 138:131127

REFERENCE 2: 137:337685

REFERENCE 3: 137:109489

REFERENCE 4: 137:24314

REFERENCE 5: 136:406945

REFERENCE 6: 136:355482

REFERENCE 7: 136:325420

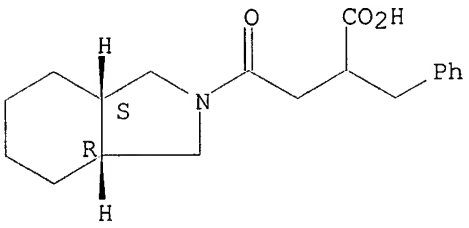
REFERENCE 8: 136:252567

REFERENCE 9: 136:205430

REFERENCE 10: 136:205424

L72 ANSWER 3 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 145324-18-1 REGISTRY
CN **2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, cis- (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C19 H25 N O3**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Relative stereochemistry.



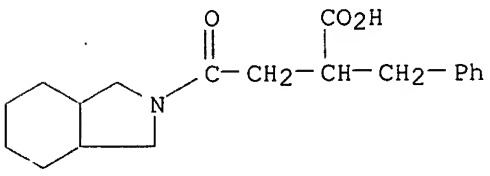
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1962 TO DATE)
2 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 127:307269

REFERENCE 2: 118:59584

L72 ANSWER 4 OF 4 REGISTRY COPYRIGHT 2003 ACS
RN 145324-16-9 REGISTRY
CN **2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI)** (CA INDEX NAME)
FS 3D CONCORD
MF **C19 H25 N O3**
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 118:59584

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 17:41:22 ON 04 MAR 2003
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FILE COVERS 1907 - 4 Mar 2003 VOL 138 ISS 10
FILE LAST UPDATED: 3 Mar 2003 (20030303/ED)

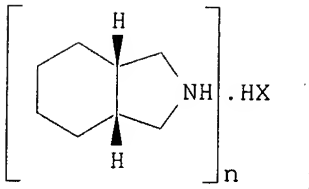
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all hitstr tot 166

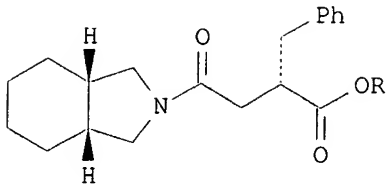
L66 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:704720 HCAPLUS
DN 135:272868
TI Preparation of hexahydroisoindolin acid addition salt and its use for synthesis of benzylsuccinic acid derivative
IN Kamijo, Tetsukiyo; Yanagi, Takashi; Kikuchi, Takeshi
PA Kissei Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-44
ICS A61P003-10; A61K031-4035; C07M007-00
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2001261644	A2	20010926	JP 2000-80736	20000322 <--
PRAI	JP 2000-80736		20000322 <--		

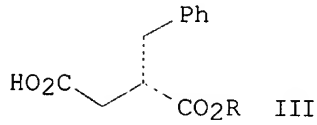
OS CASREACT 135:272868; MARPAT 135:272868
GI



I



II



III

AB Cis-hexahydroisoindolin acid addn. salts (I; X = phosphoric acid or acetic acid residue; n = 1,2; provided that when X is acetic acid residue, n represents 1) are prepd. and used for the synthesis of .alpha.-benzylsuccinic acid deriv. (II; R = H) by condensation of I with reactive, functionalized derivs. of .alpha.-benzylsuccinic acid mono esters (III; R = carboxy-protecting group) in the presence of a basic substance followed by deprotection. II (R = H) possess hypoglycemic activity and are useful for the treatment of **diabetes** (no data). Thus, 5.00 g cis-hexahydroisoindolin contg. 1.93% trans-hexahydroisoindolin was dissolved in 20 mL methylcyclohexane and 25 mL denatured ethanol, followed by adding dropwise 4.60 g 85% H3PO4 at 65.degree. under stirring, and the resulting soln. was seeded and cooled with stirring. The pptd. crystals were collected by filtration and washed with a 1:1 mixt. of methylcyclohexane and denatured ethanol (10 mL) to give 7.84 g cis-hexahydroisoindolin monophosphate contg. 0.17% trans-hexahydroisoindolin which (5.00 g) was recrystd. from 22 mL methylcyclohexane and 0.28 mL H2O to give 4.81 g cis-hexahydroisoindolin monophosphate contg. 0.03% trans-hexahydroisoindolin. (3S)-3-methoxycarbonyl-4-phenylbutanoic acid (4.98 g) was dissolved in 30 mL toluene, treated with 0.10 mL DMF and 1.95 mL SOCl2 with stirring under ice-cooling, and stirred for 5 min under ice-cooling to give a soln. of (3S)-3-methoxycarbonyl-4-phenylbutanoyl chloride. The latter soln. was added dropwise to a soln. of 5.50 g cis-hexahydroisoindolin monophosphate contg. 0.02% trans-hexahydroisoindolin (prepn. given in another example) and 15.5 g K2CO3 in 60 mL H2O for a period of 20 min with stirring under ice-cooling, and the resulting mixt. was stirred under ice-cooling for 30 min and at room temp. for 30 min to give 7.38 g II (R = Me). II (R = Me) (7.38 g) was dissolved in 17 mL isopropanol, treated with 26 mL 1 M aq. NaOH, and stirred at room temp. overnight, treated with 60 mL and then dropwise with a soln. of 1.60 g CaCl2 in 10 mL H2O at 45.degree., stirred at 45.degree. for 1 h, cooled to room temp., and stirred overnight to give, after removing the pptd. crystals by filtration and washing with 50 mL H2O, 6.95 g of white crystals. The cryst. product (5.00 g) was recrystd. from MeOH/H2O to give 4.45 g II.1/2Ca.2H2O (R = H).

ST hexahydroisoindolin acid addn salt prepn intermediate hypoglycemic; benzylhexahydroisoindolinylcarbonylpropanoic acid prepn hypoglycemic

IT **Antidiabetic** agents
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT 361342-67-8P
RL: PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT 1470-99-1P 363179-52-6P 363179-53-7P 363179-54-8P
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT 182247-45-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT 361342-63-4P **363179-56-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

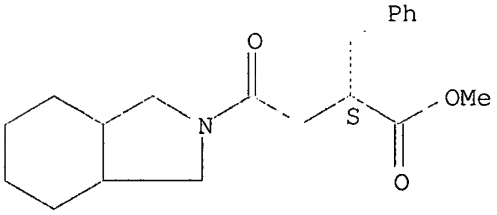
IT 10479-63-7
RL: REM (Removal or disposal); PROC (Process)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT 363179-55-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

IT **363179-56-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydroisoindolin acid addn. salt and use for synthesis of hypoglycemic benzyl(hexahydroisoindolinylcarbonyl)propanoic acid)

RN 363179-56-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, methyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

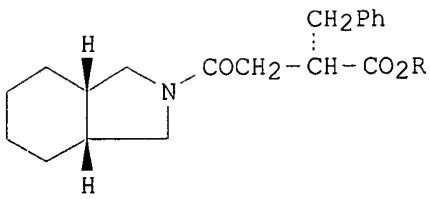


L66 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:703440 HCAPLUS
DN 135:257149
TI (3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and preparation of **antidiabetic** benzylsuccinic acid derivative therefrom
IN Kamijo, Tetsukiyo; Yanagi, Takashi; Kikuchi, Takeshi
PA Kissei Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-44
ICS C07C069-738
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001261645	A2	20010926	JP 2000-80765	20000322 <--
PRAI JP 2000-80765		20000322 <--		

OS CASREACT 135:257149

GI



III

AB (3S)-Methoxycarbonyl-4-phenylbutyric acid chloride (I) is treated with cis-hexahydroisoindoline (II) or their acid addn. salts in the presence or absence of basic substances and the resulting Me benzylsuccinate deriv. III (R = Me) (IV) is hydrolyzed and optionally neutralized or salt exchanged to give an **antidiabetic** III (R = H) (V). A toluene soln. of (3S)-methoxycarbonyl-4-phenylbutyric acid was treated with DMF and SOCl2 at 0.degree. for 5 min and at room temp. for 30 min. A toluene soln. of the resulting I was added dropwise to an aq. soln. of II phosphate and K2CO3 over 20 min and the reaction mixt. was further stirred at room temp. for 30 min to give IV. IV was treated with NaOH in Me2CHOH at room temp. overnight and further treated with CaCl2 at 45.degree. for 1 h and let stand under stirring overnight to give V.

ST **antidiabetic** benzylsuccinic acid deriv prepn; methoxycarbonylphenylbutyric chloride acylation hexahydroisoindoline

IT **Antidiabetic** agents
((3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and prepn. of **antidiabetic** benzylsuccinic acid deriv. therefrom)

IT 361342-63-4P **361342-69-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
((3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and prepn. of **antidiabetic** benzylsuccinic acid deriv. therefrom)

IT 361342-71-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
((3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and prepn. of **antidiabetic** benzylsuccinic acid deriv. therefrom)

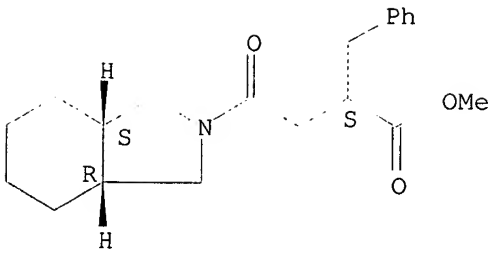
IT 1470-99-1, cis-Hexahydroisoindoline 182247-45-6 361342-67-8
RL: RCT (Reactant); RACT (Reactant or reagent)
((3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and prepn. of **antidiabetic** benzylsuccinic acid deriv. therefrom)

IT **361342-69-0P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
((3S)-Methoxycarbonyl-4-phenylbutyric acid chloride and prepn. of **antidiabetic** benzylsuccinic acid deriv. therefrom)

RN 361342-69-0 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, methyl ester, (.alpha.R,3aS,7aR)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L66 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 2001:635931 HCAPLUS
DN 135:185506
TI **Antidiabetic** agents containing .alpha.-glucosidase inhibitors and insulin secretion promoters
IN Sugiyama, Yasuo; Odaka, Hiroyuki; Sakiyama, Hiroshi; Iwasaki, Masato; Funatsu, Masami
PA Takeda Chemical Industries, Ltd., Japan
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT **Patent**
LA Japanese
IC ICM A61K045-06
ICS A61K031-44; A61K031-405; A61K031-198; A61K031-702; A61K031-133; A61K031-70; A61P003-10; A61P043-00
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001062295	A1	20010830	WO 2001-JP1282	20010222 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	JP 2001316293	A2	20011113	JP 2001-47695	20010223 <--
	US 2003040490	A1	20030227	US 2002-204783	20020821 <--
PRAI	JP 2000-52297	A	20000224 <--		
	WO 2001-JP1282	W	20010222		

AB Drugs contg., as the active ingredients, exclusively a combination of an .alpha.-glucosidase inhibitor with a non-sulfonylurea insulin secretion promoter, are useful as preventives and remedies for **diabetes**, etc. **Diabetic** patients were administered with a tablet contg. 0.2 mg voglibose and a tablet contg. 2 mg repaglinide before breakfast and blood samples were taken 1 h after meals and the results showed a significant decrease in blood glucose levels.
ST **antidiabetic** glucosidase inhibitor insulin secretion promoter; voglibose repaglinide **diabetes** control
IT **Antidiabetic** agents
(**antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)
IT Drug delivery systems
(tablets; **antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)
IT 56180-94-0, Acarbose 72432-03-2, Miglitol 80879-63-6, Emiglitate

83480-29-9, Voglibose 105816-04-4, Nateglinide 135062-02-1, Repaglinide **145375-43-5**, Mitiglinide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)

IT 9001-42-7, .alpha.-Glucosidase 9004-10-8, Insulin, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)

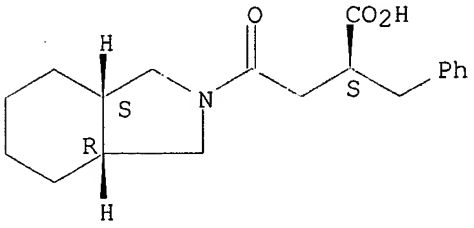
IT 50-99-7, D-Glucose, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(blood; **antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) American Chemical Society; Database CAPLUS on STN
(2) Nick, P; Formulary 1998, V33(9), P858
(3) Novo Nordisk AS; EP 1056775 A1 HCAPLUS
(4) Novo Nordisk AS; WO 9943708 A1 1999 HCAPLUS
(5) Pfizer Inc; JP 3068200 B HCAPLUS
(6) Pfizer Inc; EP 832066 A1 HCAPLUS
(7) Pfizer Inc; WO 9639385 A1 1996 HCAPLUS
(8) Smithkline Beecham P L C; EP 1001784 A1 HCAPLUS
(9) Smithkline Beecham P L C; WO 9903478 A1 1999 HCAPLUS

IT **145375-43-5**, Mitiglinide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**antidiabetic** agents contg. .alpha.-glucosidase inhibitors and insulin secretion promoters)

RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

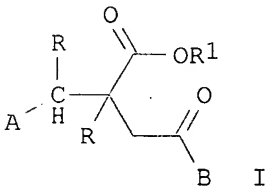


L66 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 2000:814308 HCAPLUS
DN 133:359230
TI Use of succinic acid derivatives to obtain a medicine for treating **inflammation**
IN **Caille, Dominique**
PA **Sanofi-Synthelabo, Fr.**
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT **Patent**
LA French
IC ICM A61K031-4035

ICS A61P029-00
CC 1-7 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000067752	A1	20001116	WO 2000-FR1246	20000509 <--
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2793411	A1	20001117	FR 1999-5978	19990511 <--
	FR 2793411	B1	20010629		
	EP 1178794	A1	20020213	EP 2000-927322	20000509 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002544163	T2	20021224	JP 2000-616778	20000509 <--
PRAI	FR 1999-5978	A	19990511 <--		
	WO 2000-FR1246	W	20000509 <--		

OS MARPAT 133:359230
GI



I

AB The invention concerns the use of succinic acid derivs. of general formula (I) wherein: A represents a Ph group optionally substituted by one, two or three substituents selected among a halogen, a C1-6 alkyl, C1-6 alkoxy group; a Ph, furyl, pyridyl or cycloalkyl with 3 to 8 carbon atoms; B represents an aminobicyclic group which consists of an amino cyclic compd. with 5 or 6 members condensed with a cycloalkyl ring with 5 or 6 members which may have 1 or 2 unsatd. bonds, provided that B is bound to the carbon atom of the carbonyl group on the nitrogen atom; each R represents a hydrogen atom and all the R radicals are combined together to form a chem. bond; R1 represents a hydrogen atom, a C1-6 alkyl group, an aralkyl group with 7 to 10 carbon atoms; when there exist geometric isomers, each geometric isomer, the isomers E and the isomers Z thereof, the isomers trans and the isomers cis, for treating **inflammation**. The compns. are administered at a daily dose of 1-100 mg orally, or 0.1-100 mg parenterally (no data).

ST succinic acid deriv **inflammation** inhibitor

IT Nerve, disease
(**diabetic** neuropathy; use of succinic acid derivs. to obtain medicine for treating **inflammation**)

IT **Arthritis**
(**polyarthritis**, inhibitors; use of succinic acid derivs. to obtain medicine for treating **inflammation**)

IT **Analgesics**
Anti-inflammatory agents
Antipyretics
(use of succinic acid derivs. to obtain medicine for treating

inflammation)

IT 110-15-6D, Succinic acid, derivs. **145375-43-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of succinic acid derivs. to obtain medicine for treating **inflammation)**

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

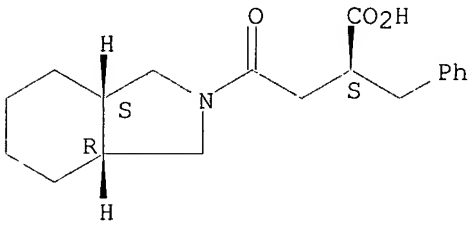
RE

(1) Adir; FR 2765578 A 1999 HCAPLUS
(2) Kissei Pharmaceutical; EP 0507534 A 1992 HCAPLUS
(3) Synthelabo; WO 9634870 A 1996 HCAPLUS

IT **145375-43-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(use of succinic acid derivs. to obtain medicine for treating **inflammation)**

RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L66 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1999:620998 HCAPLUS
DN 131:317733
TI Inhibition of heterologously expressed cystic fibrosis transmembrane conductance regulator Cl- channels by non-sulphonylurea hypoglycemic agents
AU Cai, Z.; Lansdell, K. A.; Sheppard, D. N.
CS Human Genetics Unit, Department of Medical Sciences, Molecular Medicine Centre, Western General Hospital, University of Edinburgh, Edinburgh, EH4 2XU, UK
SO British Journal of Pharmacology (**1999**), 128(1), 108-118
CODEN: BJPCBM; ISSN: 0007-1188
PB Stockton Press
DT Journal
LA English
CC **1-12** (Pharmacology)
AB Hypoglycemia-inducing sulfonylureas, such as glibenclamide, inhibit cystic fibrosis transmembrane conductance regulator (CFTR) Cl- channels. In search of modulators of CFTR, we investigated the effects of the non-sulfonylurea hypoglycemic agents meglitinide, repaglinide, and mitiglinide (KAD-1229) on CFTR Cl- channels in excised inside-out membrane patches from C127 cells expressing wild-type human CFTR. When added to the intracellular soln., meglitinide and mitiglinide inhibited CFTR Cl- currents with half-maximal concns. of 164.+-.19 .mu.M and 148.+-.36 .mu.M, resp. However, repaglinide only weakly inhibited CFTR Cl- currents. To understand better how non-sulfonylurea hypoglycemic agents inhibit CFTR, we studied single channels. Channel blockade by both meglitinide and mitiglinide was characterized by flickery closures and a significant

decrease in open probability (Po). In contrast, repaglinide was without effect on either channel gating or Po, but caused a small decrease in single-channel current amplitude. Anal. of the dwell time distributions of single channels indicated that both meglitinide and mitiglinide greatly decreased the open time of CFTR. Mitiglinide-induced channel closures were about 3-fold longer than those of meglitinide. Inhibition of CFTR by meglitinide and mitiglinide was voltage-dependent: at pos. voltages channel blockade was relieved. The data demonstrate that non-sulfonylurea hypoglycemic agents inhibit CFTR. This indicates that these agents have a wider specificity of action than previously recognized. Like glibenclamide, non-sulfonylurea hypoglycemic agents may inhibit CFTR by occluding the channel pore and preventing Cl- permeation.

ST CFTR chloride channel nonsulfonylurea hypoglycemic; glibenclamide cystic fibrosis transmembrane conductance regulator; meglitinide CFTR chloride channel; mitiglinide CFTR chloride channel

IT **Antidiabetic** agents
(inhibition of heterologously expressed cystic fibrosis transmembrane conductance regulator Cl- channels by non-sulfonylurea hypoglycemic agents)

IT CFTR (cystic fibrosis transmembrane conductance regulator)
Chloride channel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(inhibition of heterologously expressed cystic fibrosis transmembrane conductance regulator Cl- channels by non-sulfonylurea hypoglycemic agents)

IT 54870-28-9, Meglitinide 135062-02-1, Repaglinide **145375-43-5**, Mitiglinide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of heterologously expressed cystic fibrosis transmembrane conductance regulator Cl- channels by non-sulfonylurea hypoglycemic agents)

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Aguilar-Bryan, L; Science 1995, V268, P423 HCAPLUS
(2) Akiyoshi, M; Am J Physiol 1995, V268, PE185 HCAPLUS
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(8) Edwards, G; Annu Rev Pharmacol Toxicol 1993, V33, P597 HCAPLUS
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(33) Schultz, B; Am J Physiol 1996, V271, PL192 HCAPLUS
(34) Schwanstecher, M; Br J Pharmacol 1994, V113, P903 HCAPLUS
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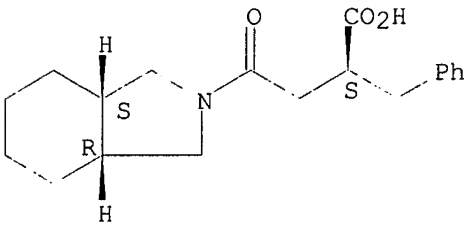
(42) Winter, M; Biophys J 1994, V66, P1398 HCAPLUS
(43) Woodhull, A; J Gen Physiol 1973, V61, P687 HCAPLUS

IT **145375-43-5**, Mitiglinide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibition of heterologously expressed cystic fibrosis transmembrane conductance regulator Cl- channels by non-sulfonylurea hypoglycemic agents)

RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

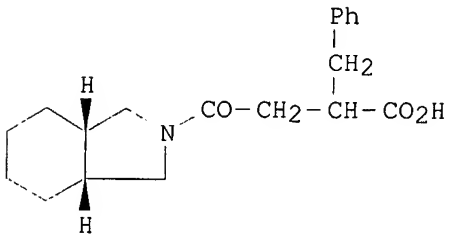


L66 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:527315 HCAPLUS
DN 129:148907
TI Process for producing benzylsuccinic acid derivatives
IN Kamijo, Tetsuhide; Yamaguchi, Toshiaki; Yanagi, Takashi
PA Kissei Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT **Patent**
LA Japanese
IC ICM C07D209-44
CC 27-10 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9832736	A1	19980730	WO 1998-JP231	19980122 <--

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9855759 A1 19980818 AU 1998-55759 19980122 <--
EP 967204 A1 19991229 EP 1998-900692 19980122 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, FI
PRAI JP 1997-50839 19970129 <--
WO 1998-JP231 19980122 <--
OS MARPAT 129:148907
GI



I

AB A novel prodn. process comprises reacting benzylsuccinic acid deriv. I with a benzyl halide such as benzyl bromide to give a benzyl ester deriv., purifying and debenzylating said deriv., followed optionally by the conversion of the products into salts, to give highly pure I or salts thereof, useful as remedies for **diabetes**. The title process provides a highly efficient purifn. method for I.

ST isoindolinylcarbonylpropionate purifn **antidiabetic**

IT **Antidiabetic** agents
(process for producing benzylsuccinic acid derivs. as **antidiabetics**)

IT Purification
(process for purifn. of benzylsuccinic acid derivs. as **antidiabetics**)

IT **145324-19-2P**
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing benzylsuccinic acid derivs.)

IT 145525-41-3P
RL: IMF (Industrial manufacture); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(process for producing benzylsuccinic acid derivs.)

IT **145375-43-5P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing benzylsuccinic acid derivs.)

IT 100-39-0, Benzyl bromide 100-51-6, Benzyl alcohol, reactions 1470-99-1 3972-36-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for producing benzylsuccinic acid derivs.)

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Kissei Pharmaceutical Co Ltd; JP 04330055 A 1992 HCAPLUS
(2) Kissei Pharmaceutical Co Ltd; JP 04330055 A 1992 HCAPLUS
(3) Kissei Pharmaceutical Co Ltd; JP 04356459 A 1992 HCAPLUS
(4) Kissei Pharmaceutical Co Ltd; JP 04356459 A 1992 HCAPLUS
(5) Kissei Pharmaceutical Co Ltd; JP 05230019 A 1992 HCAPLUS
(6) Kissei Pharmaceutical Co Ltd; JP 05230019 A 1992 HCAPLUS

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(8) Kissei Pharmaceutical Co Ltd; CA 2062877 A 1992 HCAPLUS
(9) Kissei Pharmaceutical Co Ltd; EP 507534 A1 1992 HCAPLUS
(10) Kissei Pharmaceutical Co Ltd; EP 507534 A1 1992 HCAPLUS
(11) Kissei Pharmaceutical Co Ltd; US 5202335 A 1992 HCAPLUS
(12) Kissei Pharmaceutical Co Ltd; US 5202335 A 1992 HCAPLUS
(13) Kissei Pharmaceutical Co Ltd; DK 9200415 A 1992 HCAPLUS
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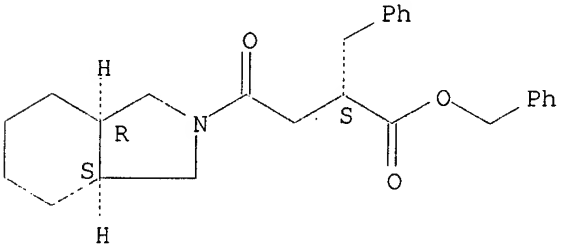
(15) Kissei Pharmaceutical Co Ltd; NO 9201200 A 1992 HCAPLUS
(16) Kissei Pharmaceutical Co Ltd; NO 9201200 A 1992 HCAPLUS
(17) Kissei Pharmaceutical Co Ltd; FI 9201392 A 1992
(18) Kissei Pharmaceutical Co Ltd; FI 9201392 A 1992
(19) Kissei Pharmaceutical Co Ltd; AU 9212809 A 1992 HCAPLUS
(20) Kissei Pharmaceutical Co Ltd; AU 9212809 A 1992 HCAPLUS
(21) Kissei Pharmaceutical Co Ltd; JP 06340622 1994 HCAPLUS
(22) Kissei Pharmaceutical Co Ltd; JP 06340623 A 1994 HCAPLUS

IT **145324-19-2P**
RL: IMF (Industrial manufacture); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing benzylsuccinic acid derivs.)

RN 145324-19-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, phenylmethyl ester, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

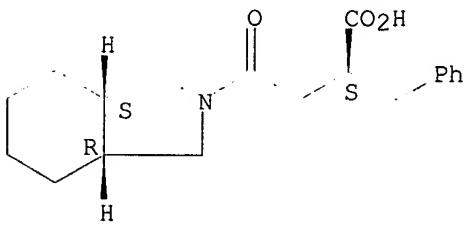
Absolute stereochemistry.



IT **145375-43-5P**
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing benzylsuccinic acid derivs.)

RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L66 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:527305 HCAPLUS
DN 129:135981
TI Process for producing optically active benzylsuccinic acid by optical

resoln.
IN Kamijo, Tetsuhide; Yamaguchi, Toshiaki; Yanagi, Takashi
PA Kissei Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DT **Patent**
LA Japanese
IC ICM C07C057-34
ICS C07C051-42; C07B057-00; C07M007-00
CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
FAN.CNT 1

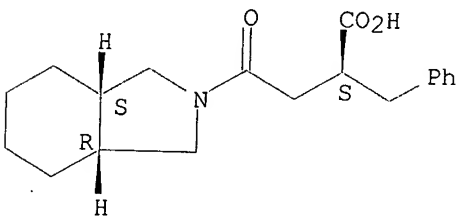
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9832727	A1	19980730	WO 1998-JP230	19980122 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9855758	A1	19980818	AU 1998-55758	19980122 <--
PRAI	JP 1997-46872		19970124 <--		
	WO 1998-JP230		19980122 <--		

AB Characterized is a process for producing the optically active (S)-benzylsuccinic acid, which is useful as a starting material for the prepn. of **diabetic** remedy, from a mixt. of corresponding optical isomers through optical resoln. using as an optical resolving agent, an org. amine selected among (R)-1-(1-naphthyl)ethylamine, (R)-.alpha.-methylbenzylamine, (S)-1-phenyl-2-(p-tolyl)ethylamine, and quinine. The optically active benzylsuccinic acid having a high optical purity and a high chem. purity can be efficiently obtained by the method of optical resoln.

ST benzylsuccinic acid prepn optical resoln amine
IT Resolution (separation)
(process for producing optically active benzylsuccinic acid by optical resoln.)
IT Amines, reactions
RL: MSC (Miscellaneous); RCT (Reactant); RACT (Reactant or reagent)
(process for producing optically active benzylsuccinic acid by optical resoln.)
IT 3972-36-9P, (S)-Benzylsuccinic acid
RL: IMF (Industrial manufacture); PUR (Purification or recovery); PREP (Preparation)
(process for producing optically active benzylsuccinic acid by optical resoln.)
IT 210710-52-4P 210710-53-5P 210710-54-6P 210710-55-7P 210710-56-8P 210710-57-9P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(process for producing optically active benzylsuccinic acid by optical resoln.)
IT **145375-43-5P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for producing optically active benzylsuccinic acid by optical resoln.)
IT 130-95-0 884-33-3 3886-69-9 3886-70-2 5267-64-1 30339-30-1, (S)-1-Phenyl-2-(p-tolyl)ethylamine 56613-80-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(process for producing optically active benzylsuccinic acid by optical resoln.)
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Hiroyuki, N; JP 59170036 A 1984 HCAPLUS
(2) K K Kankyo Kagaku Center; JP 578276 A 1993
(3) Nippon Chemipher Co Ltd; JP 5890573 A 1983
(4) Paz Arzneimittel-Entwicklungsg Mbh; EP 362476 A1 1991 HCAPLUS
(5) Paz Arzneimittel-Entwicklungsg Mbh; DE 3824353 A1 1991 HCAPLUS
(6) Paz Arzneimittel-Entwicklungsg Mbh; US 4983765 A 1991 HCAPLUS
(7) Sumitomo Chemical Co Ltd; JP 55118456 A 1980 HCAPLUS
(8) Sumitomo Chemical Co Ltd; JP 5663940 A 1981
(9) Sumitomo Chemical Co Ltd; EP 208948 A1 1986 HCAPLUS
(10) Sumitomo Chemical Co Ltd; GB 2176786 A 1986 HCAPLUS
(11) Sumitomo Chemical Co Ltd; US 4752417 A 1986 HCAPLUS
(12) Sumitomo Chemical Co Ltd; JP 61293949 A 1986 HCAPLUS
(13) Teikoku Chemical Industries Co Ltd; JP 07149688 A 1995 HCAPLUS
(14) Tosoh Corp; JP 276838 A 1990
IT **145375-43-5P**
RL: PNU (Preparation, unclassified); PREP (Preparation)
(process for producing optically active benzylsuccinic acid by optical resoln.)
RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L66 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1998:379748 HCAPLUS
DN 129:27913
TI Preparation of optically active succinic acid derivatives. III. Regioselective condensation reactions of optically active 2-substituted succinic acids with diimidazolide
AU Yamaguchi, Toshiaki; Yanagi, Takashi; Hokari, Hiroshi; Mukaiyama, Yoko; Kamijo, Tetsuhide; Yamamoto, Iwao
CS Central Research Laboratories, Kissei Pharmaceutical Co., Ltd., Nagano, 399-8304, Japan
SO Yakugaku Zasshi (**1998**), 118(6), 248-255
CODEN: YKKZAJ; ISSN: 0031-6903
PB Pharmaceutical Society of Japan
DT Journal
LA Japanese
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
OS CASREACT 129:27913
AB We investigated the large scale synthesis of monocalcium bis[(2S)-2-benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionate] dihydrate (KAD-1229), which has a potent hypoglycemic effect, in a single reaction vessel. (2S)-2-Benzyl-3-(cis-hexahydroisoindolin-2-ylcarbonyl)propionic acid was obtained from (S)-2-benzylsuccinic acid (2) and cis-hexahydroisoindoline (4), without the isolation of intermediates by the method using thionyldiimidazole (9) and/or diimidazolide of the acid 2. Sequential reaction of imidazole with thionyl chloride, 2, and 4, followed by acid catalyzed hydrolysis gave amide-carboxylic acid 7 in 86% overall yield. The acid 7 was treated with 2 N NaOH, followed by the

treatment with calcium chloride to give KAD-1229 in 91% yield.

ST succinic acid prepn benzylsuccinic hexahydroisoindoline diimidazolide; calcium benzylhexahydroisoindolinylcarbonylpropionate prepn hypoglycemic agent

IT **Antidiabetic** agents
Condensation reaction
(prepn. of optically active succinic acid derivs. as hypoglycemic agents by condensation of optically active 2-substituted succinic acids with diimidazolide)

IT **145375-43-5P 145375-44-6P** 207791-51-3P 207791-52-4P 207791-53-5P 207791-54-6P 207791-55-7P 207791-56-8P 207791-57-9P 207791-58-0P 207791-59-1P 207844-01-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically active succinic acid derivs. as hypoglycemic agents by condensation of optically active 2-substituted succinic acids with diimidazolide)

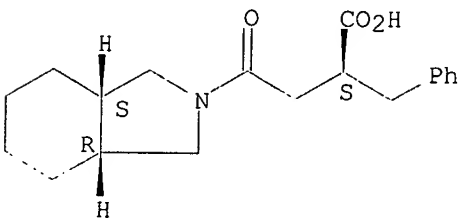
IT 110-89-4, Piperidine, reactions 110-91-8, Morpholine, reactions 288-32-4, 1H-Imidazole, reactions 597-43-3 1470-99-1, cis-Hexahydroisoindoline 2174-58-5 3972-36-9, (S)-2-Benzylsuccinic acid 46292-93-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of optically active succinic acid derivs. as hypoglycemic agents by condensation of optically active 2-substituted succinic acids with diimidazolide)

IT 161527-52-2P 161527-53-3P 207791-50-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of optically active succinic acid derivs. as hypoglycemic agents by condensation of optically active 2-substituted succinic acids with diimidazolide)

IT **145375-43-5P 145375-44-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of optically active succinic acid derivs. as hypoglycemic agents by condensation of optically active 2-substituted succinic acids with diimidazolide)

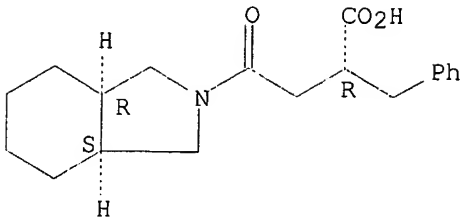
RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 145375-44-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.R,3aR,7aS)- (9CI) (CA INDEX NAME)

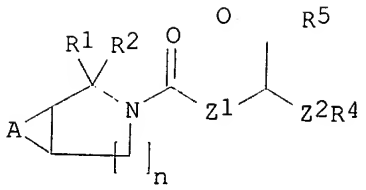
Absolute stereochemistry.



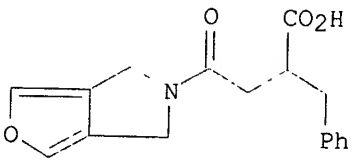
L66 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1997:34052 HCAPLUS
DN 126:59938
TI Preparation of 4-azolo-4-oxobutyrates and analogs as hypoglycemics
IN Bedoya Zurita, Manuel; Diaz Martin, Juan Antonio; Del Sol Moreno, regorio; Martin Escudero Perez, Ulpiano; Jimenez Bargueno, Maria Dolores; Romanach Ferrer, Magali
PA **Synthelabo S. A., Fr.**; Bedoya Zurita, Manuel; Diaz Martin, Juan Antonio; Del Sol Moreno, Gregorio; Martin Escudero Perez, Ulpiano; Jimenez Bargueno, Maria Dolores; Romanach Ferrer, Magali
SO PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DT **Patent**
LA French
IC ICM C07D495-04
ICS A61K031-415
CC 28-2 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9634870	A1	19961107	WO 1996-FR555	19960412 <--
	W: AL, AU, BG, BR, CA, CN, CZ, EE, FI, HU, JP, KR, LT, LV, MX, NO, NZ, PL, RU, SI, SK, TR, UA, US, VN				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	FR 2733750	A1	19961108	FR 1995-5260	19950503 <--
	FR 2733750	B1	19970613		
	CA 2220015	AA	19961107	CA 1996-2220015	19960412 <--
	AU 9656520	A1	19961121	AU 1996-56520	19960412 <--
	AU 699120	B2	19981119		
	EP 823912	A1	19980218	EP 1996-913576	19960412 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
	CN 1188478	A	19980722	CN 1996-194900	19960412 <--
	BR 9608309	A	19990126	BR 1996-8309	19960412 <--
	JP 11504913	T2	19990511	JP 1996-533065	19960412 <--
	ZA 9603485	A	19961125	ZA 1996-3485	19960502 <--
	NO 9705020	A	19980105	NO 1997-5020	19971031 <--
	US 5869518	A	19990209	US 1997-945576	19971031 <--
PRAI	FR 1995-5260		19950503 <--		
	WO 1996-FR555		19960412 <--		

OS MARPAT 126:59938
GI



I



II

AB Title compds. (I; A = atoms to form an arom. ring; R1,R2 = H, alkyl, Ph, etc.; R1R2 = O; R4 = aryl; R5 = OH, OCH2Ph, 4-methylpiperazinyl; Z1 = CHR3, O, NR3; R3 = H or alkyl; R3R4 = CH2C6H4; Z2 = CH2, O, S; n = 1 or 2) were prepd. Thus, di-Et furan-3,4-dicarboxylate was converted in 2 steps to 3,4-bis(chloromethyl)furan which was cyclocondensed with PhCONH2 to give, in 2 addnl. steps., to 5,6-dihydro-4H-furo[3,4-c]pyrrole which was amidated by Ho2CCH2C(CH2Ph)co2CH2Ph to give, after sapon., title compd. II. Data for in vivo hypoglycemic activity of I were given.

ST azolooxobutyrate prepn hypoglycemic

IT **Antidiabetic** agents
(4-azolo-4-oxobutyrates and analogs)

IT Antiobesity agents
(prepn. of 4-azolo-4-oxobutyrates and analogs as hypoglycemics)

IT 185064-97-5P 185064-98-6P 185064-99-7P 185065-00-3P 185065-01-4P
185065-02-5P 185065-03-6P 185065-04-7P **185065-05-8P**
185065-06-9P **185065-07-0P 185065-08-1P** 185065-09-2P
185065-10-5P 185065-11-6P 185065-12-7P 185065-13-8P
185065-14-9P 185065-15-0P 185065-16-1P 185065-17-2P 185065-18-3P
185065-19-4P 185065-20-7P 185065-21-8P 185065-22-9P 185065-23-0P
185065-24-1P 185065-25-2P 185065-26-3P 185065-27-4P 185065-28-5P
185065-29-6P 185065-30-9P 185065-31-0P 185065-32-1P 185065-33-2P
185065-34-3P 185065-35-4P 185065-36-5P 185065-37-6P 185065-38-7P
185065-39-8P 185065-40-1P 185065-41-2P 185065-42-3P 185065-43-4P
185065-44-5P 185065-45-6P 185065-46-7P 185065-47-8P 185065-48-9P
185065-49-0P 185065-50-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-azolo-4-oxobutyrates and analogs as hypoglycemics)

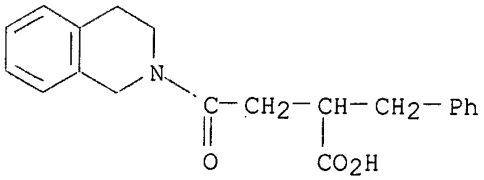
IT 55-21-0, Benzamide 91-13-4, 1,2-Bis(bromomethyl)benzene 109-01-3
496-12-8, 1H-Isoindole, 2,3-dihydro 5292-43-3, tert-Butyl bromoacetate
19438-61-0, 5-Methylisobenzofuran-1,3-dione 22767-96-0, Benzyl
3-phenylpropionate 25282-53-5 30614-77-8, Di-Ethyl
furan-3,4-dicarboxylate 140903-48-6 185065-66-1 185065-68-3
185065-69-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of 4-azolo-4-oxobutyrates and analogs as hypoglycemics)

IT 6372-18-5P, 3,4-Bis(chloromethyl)furan 14496-24-3P, Furan-3,4-dimethanol
40314-06-5P 57584-71-1P 93282-20-3P 185065-51-4P 185065-52-5P
185065-53-6P 185065-54-7P 185065-55-8P 185065-56-9P 185065-57-0P
185065-58-1P 185065-59-2P 185065-60-5P 185065-61-6P 185065-62-7P
185065-63-8P 185065-64-9P 185065-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-azolo-4-oxobutyrates and analogs as hypoglycemics)

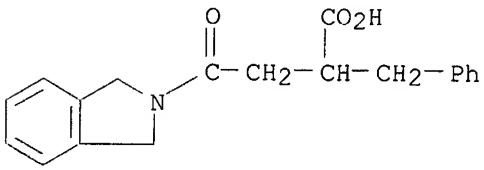
IT **185065-05-8P 185065-07-0P 185065-08-1P**
185065-10-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-azolo-4-oxobutyrates and analogs as hypoglycemics)

RN 185065-05-8 HCAPLUS

CN 2(1H)-Isoquinolinebutanoic acid, 3,4-dihydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)

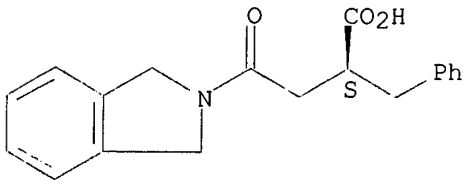


RN 185065-07-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)



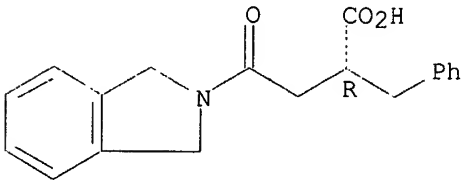
RN 185065-08-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 185065-10-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3-dihydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

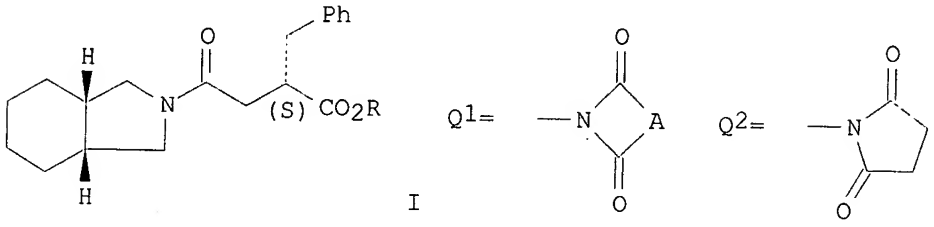


L66 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:446724 HCAPLUS
DN 122:213925
TI Preparation of hexahydroisoindoline derivative as **antidiabetic** agent
IN Kamijo, Tetsukyo; Yanagi, Takashi; Hokari, Hiroshi; Oda, Juko
PA Kissei Pharmaceutical, Japan

SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-44
ICS C07D401-12; C07D403-12
ICA A61K031-40
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

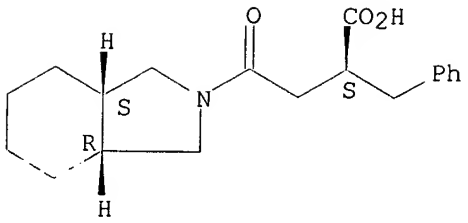
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 06340622	A2	19941213	JP 1993-165852	19930528 <--
JP 3207017	B2	20010910		

PRAI JP 1993-165852 19930528 <--
OS CASREACT 122:213925; MARPAT 122:213925
GI



AB The title compd. I [R = H], useful as an **antidiabetic** agent (no data), is prepd. by hydrolysis of hexahydroisoindoline deriv. I [R = Q1; A = ethylene, etc.]. A mixt. of I [R = Q2], methanol , and aq. sodium hydroxide was stirred for 3 h to give, after workup, 49% I [R = H].
ST isoindoline hexahydroiso prepn **antidiabetic**; sapon succinimidyl hexahydroisoindolinylcarbonylpropionate
IT Saponification
(of succinimidyl hexahydroisoindolinylcarbonylpropionate and analogs)
IT 161829-93-2P 161829-94-3P 161829-95-4P 161829-96-5P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
IT **145375-43-5P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
IT 1310-73-2, Sodium hydroxide, reactions 1470-99-1, cis-Hexahydroisoindoline 3972-36-9, (S)-Benzylsuccinic acid 21715-90-2 74124-79-1 161829-92-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
IT 161829-97-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
IT **145375-43-5P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

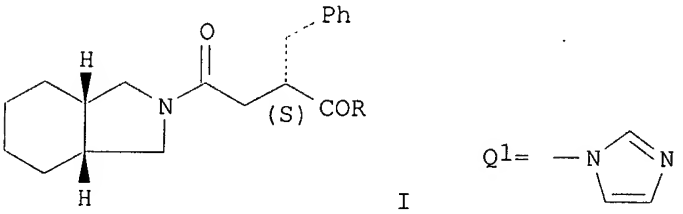
Absolute stereochemistry. Rotation (-).



L66 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1995:412896 HCAPLUS
DN 122:187390
TI Preparation of hexahydroisoindoline derivative as **antidiabetic** agent
IN Kamijo, Tetsukyo; Yanagi, Takashi; Hokari, Hiroshi; Oda, Juko
PA Kissei Pharmaceutical, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-44
ICS A61K031-40; C07D403-06
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 06340623	A2	19941213	JP 1993-165853	19930528 <--
JP 3207018	B2	20010910		
PRAI JP 1993-165853		19930528 <--		

GI



I

AB The title compd. I [R = OH], useful as an **antidiabetic** agent (no data), was prepd. by hydrolysis of I [R = Q1]. A mixt. of I [R = Q1] , Et acetate, and water contg. HCl was stirred for 1 h to give, after workup, 83% I [R = OH].

ST isoindoline hexahydro prepn **antidiabetic**; hydrolysis hexahydroisoindoline

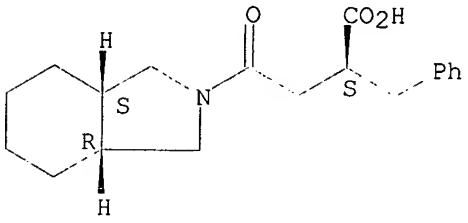
IT 161527-52-2P 161527-53-3P
RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)

IT **145375-43-5P** 145525-41-3P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)

IT 288-32-4, Imidazole, reactions 530-62-1, N,N'-Carbonyldiimidazole 1470-99-1, cis-Hexahydroisoindoline 3972-36-9, (S)-Benzylsuccinic acid
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
IT **145375-43-5P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(prepn. of hexahydroisoindoline deriv. as **antidiabetic** agent)
RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

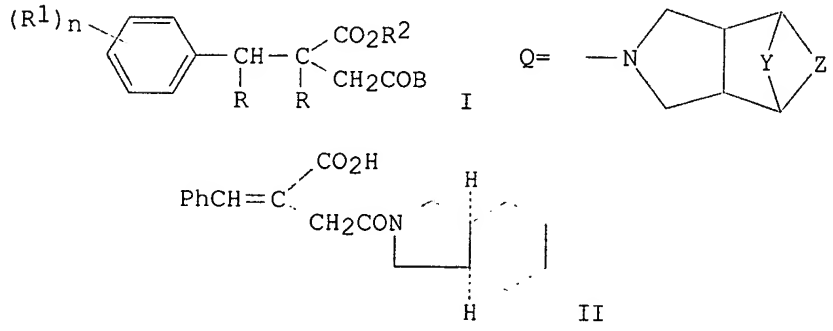
Absolute stereochemistry. Rotation (-).



L66 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:533972 HCAPLUS
DN 121:133972
TI Preparation of benzyl- and benzylidenesuccinic acid monoamide derivatives for treatment of **diabetes** mellitus
IN Sato, Fumyasu; Oonoda, Hideki; Hokari, Hiroshi; Yanagi, Takashi; Kamijo, Tetsukyo
PA Kissei Pharmaceutical, Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-72
ICS A61K031-40; C07D209-70; C07D491-18
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06107635	A2	19940419	JP 1992-300259	19920929 <--
	JP 3179895	B2	20010625		
PRAI	JP 1992-300259		19920929 <--		

OS MARPAT 121:133972
GI



I

II

AB The title compds. (I; R = H or RR forms a single bond; R1 = H, halo, C1-6 alkyl or alkoxy; R2 = H, C1-6 alkyl, C7-10 aralkyl; B = tricyclic condensed cyclic amino; n = 1,2), more specifically I (R, R1,n = same as above; R2 = H; B = Q; Y = CH2, CH2CH2, O; Z = CH2CH2, CH:CH), and salts thereof are prepd. I promote insulin secretion and lower blood sugar level. Thus, cis-hexahydro-4,7-methano-3a.alpha.,4.beta.,7.beta.,7a.alpha .-isoindoline was added dropwise to a suspension of (E)-2-benzylidenesuccinic anhydride in CH2Cl2 followed by stirring at room temp. for 2 h to give title compd. (II). I at 0.5-10 mg/kg p.o. apparently lowered blood pressure in mice.

ST benzylidenesuccinic acid monoamide prepn treatment **diabetes**; methanoisoindoline amide benzylidenesuccinic acid **antidiabetic**; benzylsuccinic acid monoamide prepn treatment **diabetes**; succinic acid monoamide prepn treatment **diabetes**; **antidiabetic** benzylidenesuccinic acid monoamide; tricyclic amine benzylsuccinic acid monoamide

IT **Antidiabetics** and Hypoglycemics
(benzyl- and benzylidenesuccinic acid monoamides with tricyclic amines)

IT 16160-75-1, cis-Hexahydro-4,7-methano-3a.alpha.,4.beta.,7.beta.,7a.alpha.-isoindoline 157060-07-6, cis-Hexahydro-4,7-ethanoisoindoline 157182-64-4 157182-65-5, cis-Hexahydro-4,7-epoxyisoindoline
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with benzylidenesuccinic anhydride)

IT 157060-08-7, cis-3a,4,7,7a-Tetrahydroisoindoline hydrochloride 157182-66-6, cis-Hexahydro-4,7-epoxyisoindoline hydrochloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with bis(nitrophenyl) benzylsuccinate)

IT 145324-57-8, (E)-(4-Chlorobenzylidene)succinic anhydride 145324-59-0, (E)-(2-Methoxybenzylidene)succinic anhydride
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with hexahydroethanoisoindoline)

IT 125702-11-6, (E)-2-Benzylidenesuccinic anhydride 140903-48-6, (S)-3-Benzyloxycarbonyl-4-phenylbutyric acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with hexahydromethanoisoindoline)

IT 123-25-1, Diethyl succinate
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzaldehyde derivs.)

IT 83-38-5, 2,6-Dichlorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with di-Et succinate)

IT 100-02-7, 4-Nitrophenol, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with benzylsuccinic acid)

IT 3972-36-9, (S)-2-Benzylsuccinic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification of, with nitrophenol)

IT 145324-43-2P, (E)-(2-Methylbenzylidene)succinic anhydride 145324-50-1P, (E)-(2,6-Dichlorobenzylidene)succinic anhydride 157060-06-5P, Bis(4-nitrophenyl) (S)-2-benzylsuccinate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation of, with tricyclic amine)

IT **157060-05-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and epoxidn. of)

IT 157060-04-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and transesterification of, with methanol)

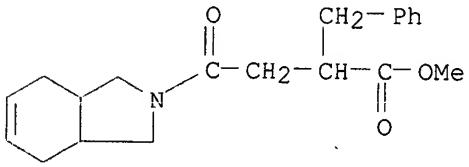
IT 157059-84-2P 157059-85-3P 157059-86-4P 157059-87-5P 157059-88-6P 157059-89-7P 157059-90-0P 157059-91-1P 157059-92-2P 157059-93-3P

157059-94-4P 157059-95-5P 157059-96-6P 157059-97-7P 157059-98-8P
157059-99-9P 157060-00-9P 157060-01-0P 157060-02-1P 157060-03-2P
157060-09-8P 157182-67-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

IT **157060-05-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and epoxidn. of)

RN 157060-05-4 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)



L66 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2003 ACS

AN 1994:508510 HCAPLUS

DN 121:108510

TI preparation of benzyl- or [(cyclic amino)carbonyl]succinic acid derivatives as **antidiabetics**

IN Sato, Fumyasu; Oonoda, Hideki; Hokari, Hiroshi; Kamijo, Tetsukyo

PA Kissei Pharmaceutical, Japan

SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF

DT **Patent**

LA Japanese

IC ICM C07D209-44
ICS A61K031-40; A61K031-435; A61K031-55; C07D209-54; C07D209-72; C07D209-96; C07D221-20; C07D223-14; C07D491-113

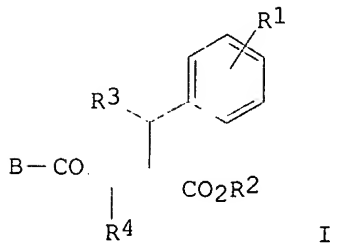
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06107633	A2	19940419	JP 1992-300262	19920929 <--
	JP 3179897	B2	20010625		
PRAI	JP 1992-300262		19920929 <--		

OS MARPAT 121:108510

GI



I

AB Title compds. I [R1 = H, C1-4 alkyl, C1-4 alkoxy; R2 = H, C1-6 alkyl; R3, R4 = H, C1-4 alkyl; however, R3 .noteq. R4; B = spiro cyclic amino,

tricyclic amino, bicyclic amino], useful as **antidiabetics** (no data), are prepd. E.g., (E)-2-benzylidene-3-(cis-hexahydro-2-isoindolinylcarbonyl)propionic acid Me ester (prepn. given) in THF was treated with lithium diisopropylamide in THF, the resulting mixt. was stirred at -70.degree., MeI was added, and the resulting mixt. was stirred for 1 h to give (E)-2-benzylidene-3-(cis-hexahydro-2-isoindolinylcarbonyl)butyric acid Me ester, which was hydrolyzed and the free acid was hydrogenated over palladium/charcoal to give I [R1 = R2 = R3 = H, R4 = Me; B = cis-hexahydro-2-isoindolinylcarbonyl].

ST succinic acid deriv prepn **antidiabetic**

IT **Antidiabetics** and Hypoglycemics
([(cyclic amino)carbonyl]succinic acid derivs.)

IT 156542-30-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

IT 156542-11-9P 156542-12-0P 156542-13-1P 156542-14-2P 156542-15-3P
156542-16-4P 156542-17-5P 156542-18-6P 156542-19-7P 156542-20-0P
156542-21-1P 156542-22-2P 156542-23-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

IT 1141-85-1P **145323-82-6P 145324-05-6P**
145324-09-0P 145324-43-2P 156542-24-4P 156542-25-5P
156542-26-6P 156542-27-7P 156542-28-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **antidiabetics**)

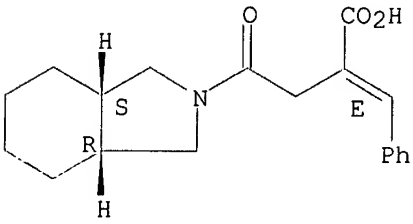
IT 123-25-1, Diethyl succinate 177-11-7, 8-Aza-1,4-dioxaspiro[4,5]decane
180-44-9, 3-Azaspiro[5,5]undecane 529-20-4, 2-Methylbenzaldehyde
1470-99-1, cis-Hexahydroisoindoline 16160-75-1 74222-66-5
125702-11-6 156542-29-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of **antidiabetics**)

IT **145323-82-6P 145324-05-6P 145324-09-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **antidiabetics**)

RN 145323-82-6 HCAPLUS

CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

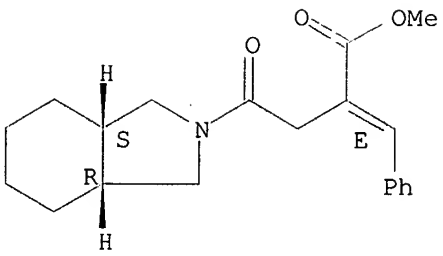
Relative stereochemistry.
Double bond geometry as shown.



RN 145324-05-6 HCAPLUS

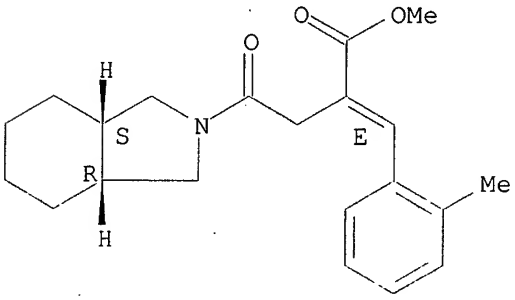
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 145324-09-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L66 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:483073 HCAPLUS
DN 121:83073
TI Preparation of benzyl- and benzylidenesuccinic acid monoamide derivatives for treatment of **diabetes** mellitus
IN Sato, Fumyasu; Oonoda, Hideki; Hokari, Hiroshi; Oda, Juko; Kamijo, Tetsukyo
PA Kissei Pharmaceutical, Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D221-20
ICS A61K031-40; A61K031-435; A61K031-55; C07D209-96; C07D223-14; C07D491-113
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06107640	A2	19940419	JP 1992-300260	19920929 <--
	JP 3179896	B2	20010625		
PRAI	JP 1992-300260		19920929 <--		

OS MARPAT 121:83073
GI For diagram(s), see printed CA Issue.
AB The title compds. (I; R = H or RR forms a single bond; R1 = H, halo, C1-6 alkyl or alkoxy; R2 = H, C1-6 alkyl; B = spirocyclic amino; n = 1,2), more specifically I (R, R1,n = same as above; R2 = H; B = Q; X = methylene, O; m = 2-4; q = 1-3), and salts thereof are prepd. I promote insulin

secretion and lower blood sugar level. Thus, 3-azaspiro[5.5]undecane was added dropwise to a suspension of (E)-2-benzylidenesuccinic anhydride in CH2Cl2 followed by stirring at room temp. for 2 h to give spiropiperidinecyclohexane deriv. (II). I at 0.5-10 mg/kg p.o. apparently lowered blood pressure in mice.

ST benzylidenesuccinic acid monoamide prepn treatment **diabetes**; spiropiperidinecyclohexane benzylidenesuccinic acid monoamide **antidiabetic**; benzylsuccinic acid monoamide prepn treatment **diabetes**; succinic acid monoamide prepn treatment **diabetes** ; **antidiabetic** benzylidenesuccinic acid monoamide; spirocyclic amine benzylsuccinic acid monoamide

IT **Antidiabetics** and Hypoglycemics
(benzyl- and benzylidenesuccinic acid monoamides with spirocyclic amines)

IT 3972-36-9, (S)-Benzylsuccinic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with azaspiroundecane)

IT 176-64-7, 8-Azaspiro[4.5]decane 177-11-7, 8-Aza-1,4-dioxaspiro[4.5]decane 180-44-9, 3-Azaspiro[5.5]undecane
RL: RCT (Reactant); RACT (Reactant or reagent)
(amidation of, with benzylidenesuccinic anhydride deriv.)

IT 123-25-1, Diethyl succinate
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with benzaldehyde derivs.)

IT 83-38-5, 2,6-Dichlorobenzaldehyde 446-52-6, 2-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 6502-22-3, 2-Isopropylbenzaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(condensation of, with di-Et succinate)

IT 334-88-3, Diazomethane
RL: RCT (Reactant); RACT (Reactant or reagent)
(esterification by, of benzylidenesuccinic acid monoamide deriv.)

IT 145324-43-2P, (E)-(2-Methylbenzylidene)succinic anhydride 145324-45-4P, (E)-(2-Isopropylbenzylidene)succinic anhydride 145324-46-5P, (E)-(2-Fluorobenzylidene)succinic anhydride 145324-50-1P, (E)-(2,6-Dichlorobenzylidene)succinic anhydride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and amidation of, with spirocyclic amines)

IT 1141-85-1P, (E)-(2-Methylbenzylidene)succinic acid
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and conversion of, into acid anhydride)

IT **156541-86-5P 156541-87-6P** 156541-88-7P
156541-89-8P 156541-90-1P 156541-91-2P
156541-92-3P 156541-93-4P 156541-94-5P
156541-95-6P 156541-96-7P 156541-97-8P
156541-98-9P 156541-99-0P **156542-00-6P**
156542-01-7P 156542-02-8P 156542-03-9P
156542-04-0P 156542-05-1P 156542-06-2P
156542-07-3P 156542-08-4P 156542-09-5P
156542-10-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

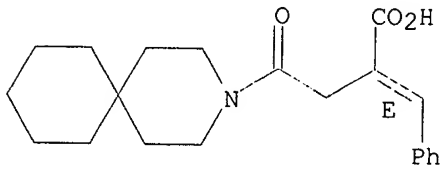
IT **156541-86-5P 156541-87-6P 156541-89-8P**
156541-90-1P 156541-91-2P 156541-92-3P
156541-93-4P 156541-94-5P 156541-95-6P
156541-96-7P 156541-97-8P 156541-98-9P
156542-00-6P 156542-01-7P 156542-02-8P
156542-04-0P 156542-05-1P 156542-06-2P
156542-07-3P 156542-08-4P 156542-09-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

RN 156541-86-5 HCAPLUS

CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .gamma.-oxo-.alpha.-

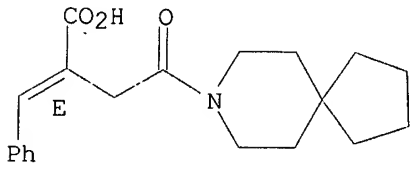
(phenylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



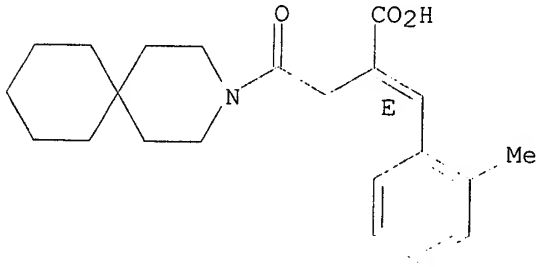
RN 156541-87-6 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethylene)-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



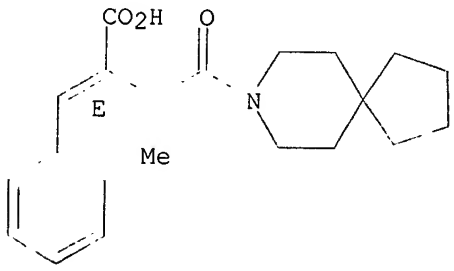
RN 156541-89-8 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 156541-90-1 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

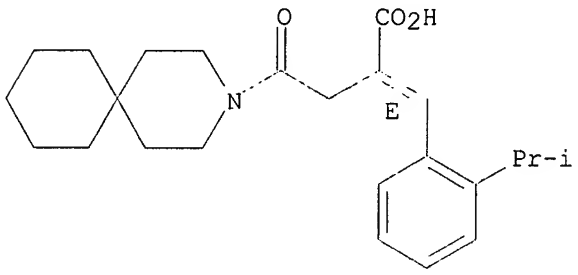
Double bond geometry as shown.



RN 156541-91-2 HCAPLUS

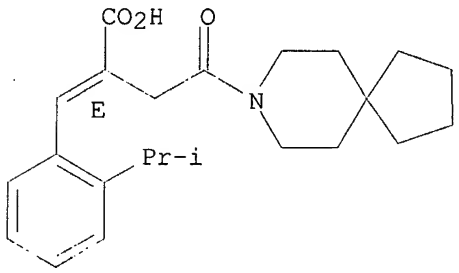
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[[2-(1-methylethyl)phenyl]methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



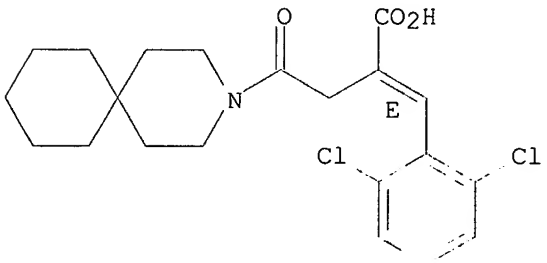
RN 156541-92-3 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[[2-(1-methylethyl)phenyl]methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



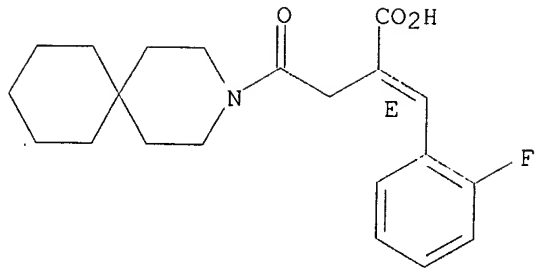
RN 156541-93-4 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2,6-dichlorophenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



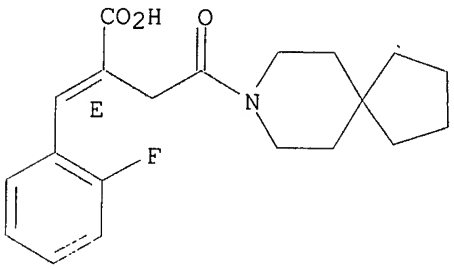
RN 156541-94-5 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-fluorophenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



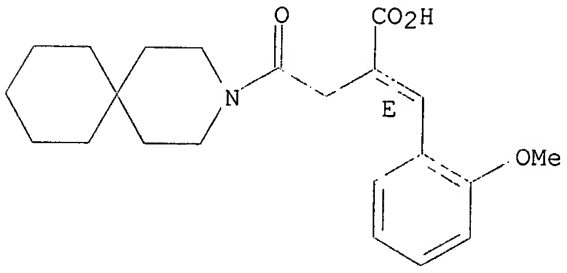
RN 156541-95-6 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[(2-fluorophenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



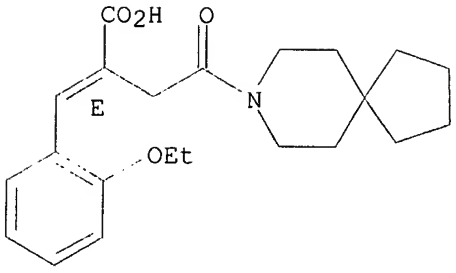
RN 156541-96-7 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-methoxyphenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



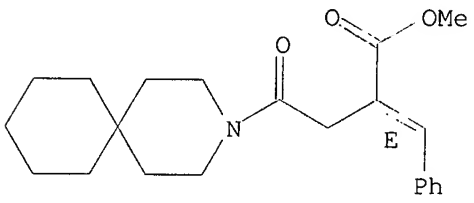
RN 156541-97-8 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[(2-ethoxyphenyl)methylene]-.gamma.-oxo-, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



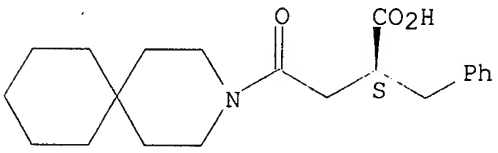
RN 156541-98-9 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethylene)-, methyl ester, (E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

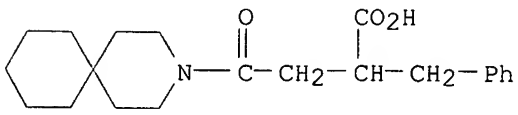


RN 156542-00-6 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, (S)- (9CI) (CA INDEX NAME)

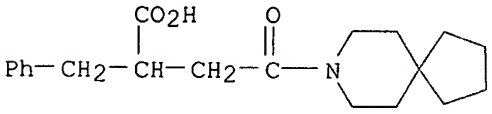
Absolute stereochemistry.



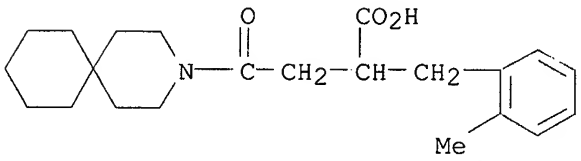
RN 156542-01-7 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)



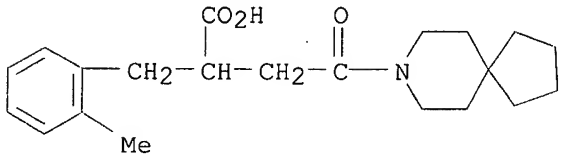
RN 156542-02-8 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-(9CI) (CA INDEX NAME)



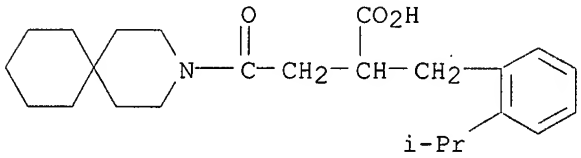
RN 156542-04-0 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



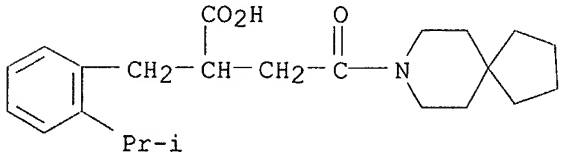
RN 156542-05-1 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



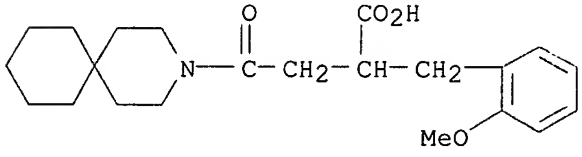
RN 156542-06-2 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[[2-(1-methylethyl)phenyl]methyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



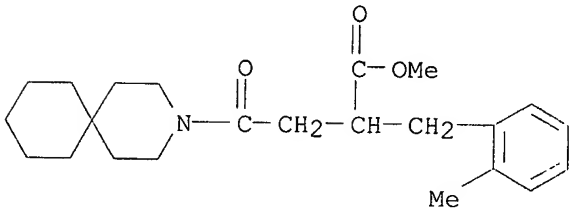
RN 156542-07-3 HCAPLUS
CN 8-Azaspiro[4.5]decane-8-butanoic acid, .alpha.-[[2-(1-methylethyl)phenyl]methyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



RN 156542-08-4 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-methoxyphenyl)methyl]-.gamma.-oxo- (9CI) (CA INDEX NAME)



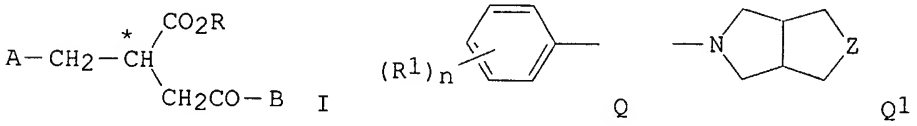
RN 156542-09-5 HCAPLUS
CN 3-Azaspiro[5.5]undecane-3-butanoic acid, .alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo-, methyl ester (9CI) (CA INDEX NAME)



L66 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1994:244117 HCAPLUS
DN 120:244117
TI Preparation of succinic acid derivatives as **antidiabetics**
IN Sato, Fumyasu; Tsubaki, Atsushi; Hokari, Hiroshi; Tanaka, Nobuyuki; Saito, Masaru; Akaha, Kenji; Kobayashi, Michihiro
PA Kissei Pharmaceutical, Japan
SO Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DT **Patent**
LA Japanese
IC ICM C07D209-44
ICS A61K031-40; C07D209-08; C07D215-06; C07D409-06
CC 23-16 (Aliphatic Compounds)
Section cross-reference(s): 1, 27
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 05294926	A2	19931109	JP 1992-143131	19920417 <--
PRAI JP 1992-143131		19920417 <--		

OS MARPAT 120:244117
GI



AB Title compds. I [A = heterocyclyl, cycloalkyl, substituted Ph, e.g., Q; R1 = halo, alkyl, alkoxy; n = 1-3 integer; B = bicyclic amino group contg. 1-2 double bonds, Q1; Z = CH2CH2, CH:CH; R = H, alkyl], useful as **antidiabetics** (no data), are prepd. E.g., (E)-(4-methylbenzylidene)succinic anhydride was reacted with cis-hexahydroisoindoline in CH2Cl2 at room temp. for 2 h to give (E)-3-(cis-hexahydro-2-isoindolinylcarbonyl)-2-(4-methylbenzylidene)propionic acid, which was hydrogenated over palladium/C at room temp. for 16 h to give 3-(cis-hexahydro-2-isoindolinylcarbonyl)-2-(4-methylbenzyl)propionic acid.
ST succinic acid deriv prepn **antidiabetic**
IT **Antidiabetics** and Hypoglycemics
(succinic acid derivs.)
IT **145324-23-8P 145324-24-9P 145324-25-0P**
145324-26-1P 145324-27-2P 145324-28-3P

145324-29-4P 145324-30-7P 145324-31-8P
145324-32-9P 145324-33-0P 145324-35-2P
145324-37-4P 145324-38-5P 145324-39-6P
145324-41-0P 145324-42-1P 154142-22-0P
154142-23-1P 154142-24-2P 154142-25-3P
154142-26-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

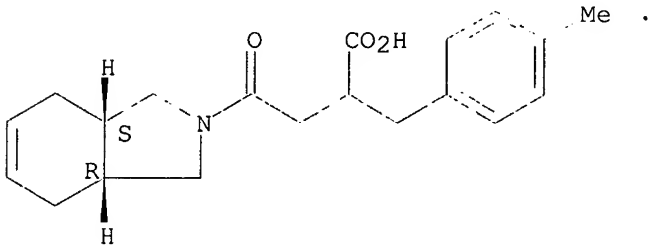
IT 6315-21-5P **145323-88-2P 145323-89-3P**
145323-90-6P 145323-91-7P 145323-92-8P
145323-96-2P 145323-97-3P 145323-98-4P
145323-99-5P 145324-01-2P 145324-02-3P 145324-03-4P
145324-43-2P 145324-44-3P 145324-45-4P 145324-47-6P 145324-48-7P
145324-49-8P 145324-51-2P 145324-52-3P 145324-54-5P 145324-55-6P
154142-27-5P 154142-28-6P 154142-29-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **antidiabetics**)

IT 100-02-7, 4-Nitrophenol, reactions 123-25-1, Succinic acid diethyl ester
529-20-4, 2-Methylbenzaldehyde 613-69-4, 2-Ethoxybenzaldehyde
620-23-5, 3-Methylbenzaldehyde 1123-56-4, 2,6-Dimethylbenzaldehyde
1470-99-1, cis-Hexahydroisoindoline 2043-61-0, Cyclohexanecarboxaldehyde
2144-87-8 3392-97-0, 2,6-Dimethoxybenzaldehyde 6502-22-3,
2-Isopropylbenzaldehyde 7091-12-5, 2-Propoxybenzaldehyde 15822-93-2
33446-22-9, 2-(4-Methylbenzylidene)succinic acid 56416-13-8,
2-(4-Chlorobenzyl)succinic acid 103857-61-0, 2-(2-Chlorobenzyl)succinic
acid 145324-56-7 145324-59-0 145324-60-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of **antidiabetics**)

IT **145324-23-8P 145324-24-9P 145324-25-0P**
145324-26-1P 145324-27-2P 145324-28-3P
145324-29-4P 145324-30-7P 145324-31-8P
145324-32-9P 145324-33-0P 145324-37-4P
145324-38-5P 145324-39-6P 145324-41-0P
145324-42-1P 154142-23-1P 154142-24-2P
154142-25-3P 154142-26-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

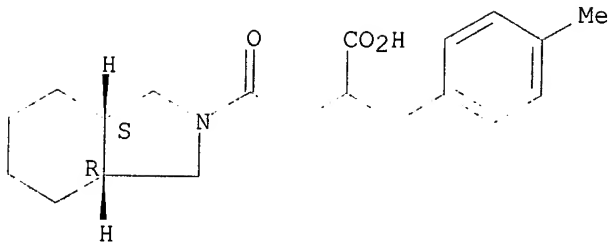
RN 145324-23-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



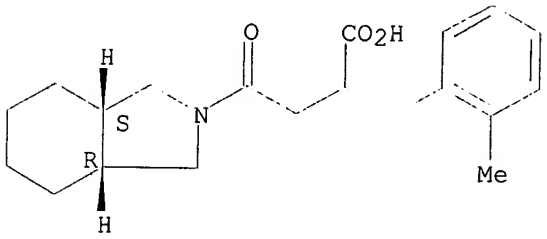
RN 145324-24-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



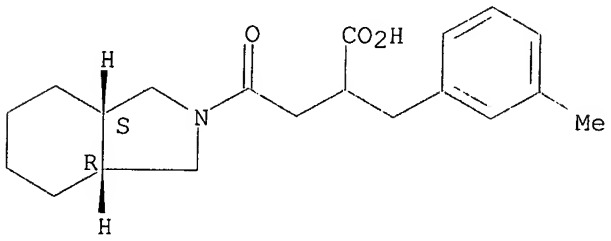
RN 145324-25-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



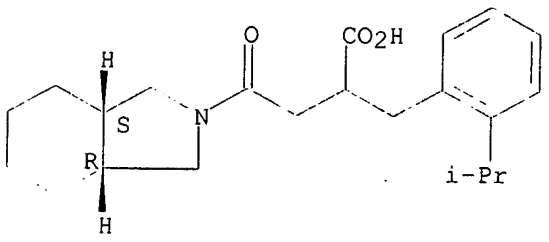
RN 145324-26-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(3-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



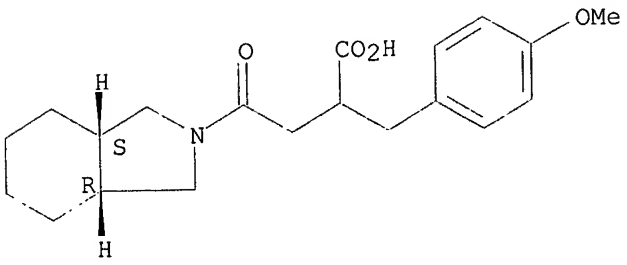
RN 145324-27-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[[2-(1-methylethyl)phenyl]methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



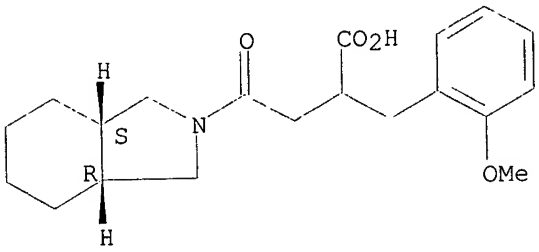
RN 145324-28-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methoxyphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



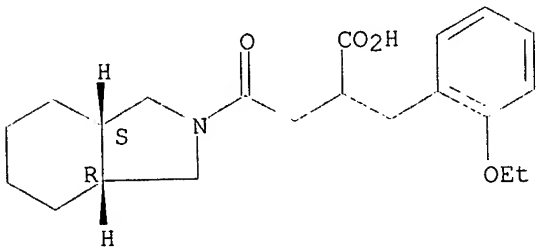
RN 145324-29-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methoxyphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



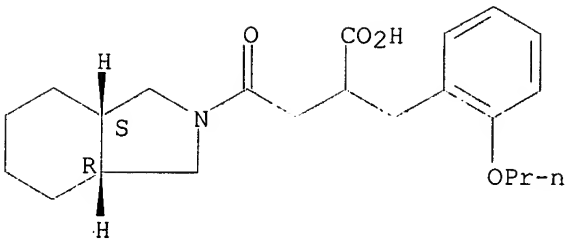
RN 145324-30-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-ethoxyphenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



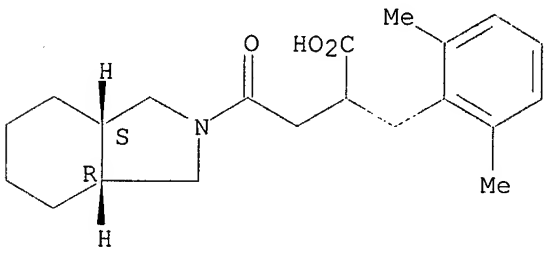
RN 145324-31-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-[(2-propoxyphenyl)methyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



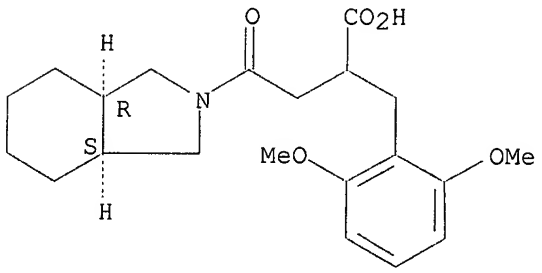
RN 145324-32-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethylphenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



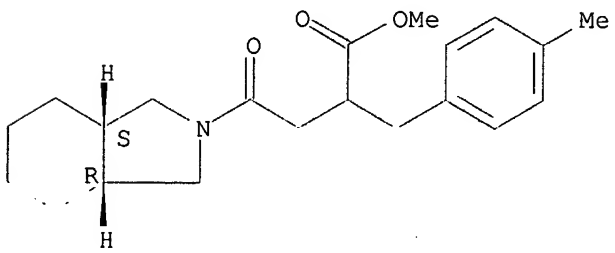
RN 145324-33-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethoxyphenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



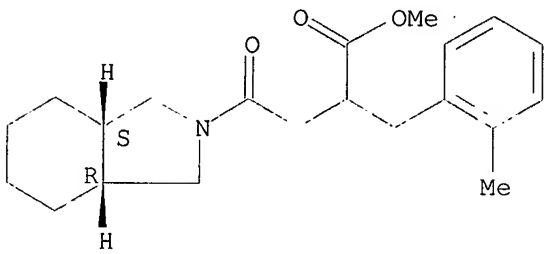
RN 145324-37-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



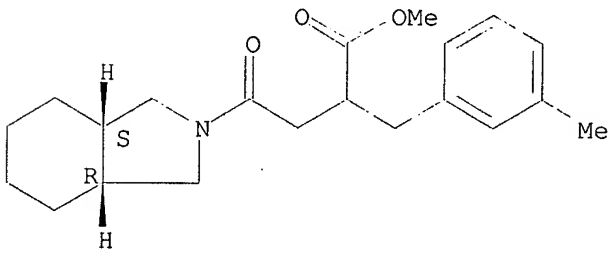
RN 145324-38-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



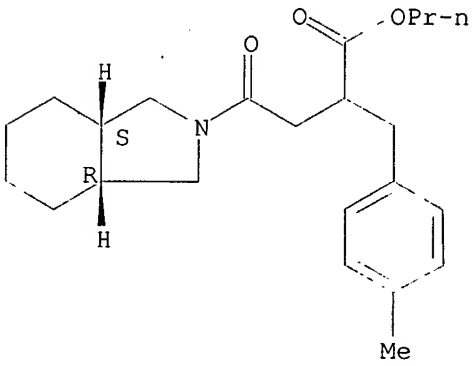
RN 145324-39-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(3-methylphenyl)methyl]-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



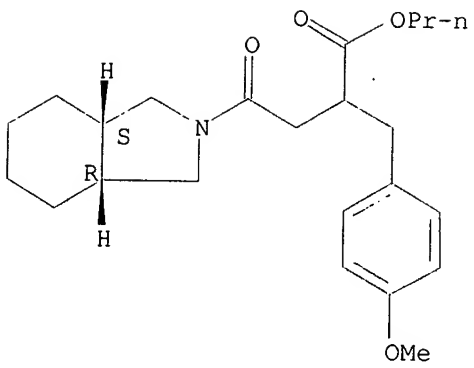
RN 145324-41-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, propyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



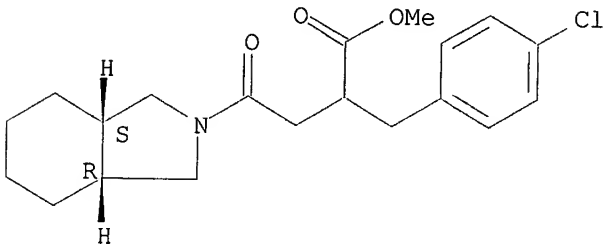
RN 145324-42-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methoxyphenyl)methyl]-.gamma.-oxo-, propyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



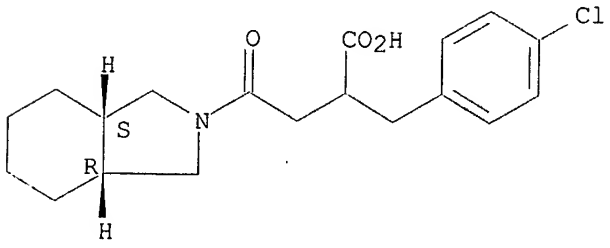
RN 154142-23-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(4-chlorophenyl)methyl]octahydro-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



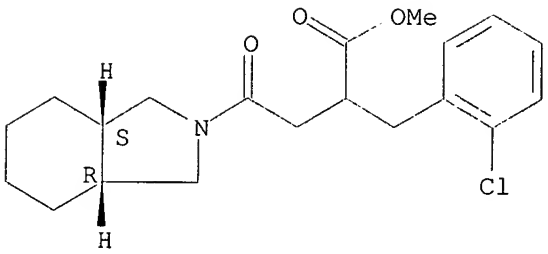
RN 154142-24-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(4-chlorophenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



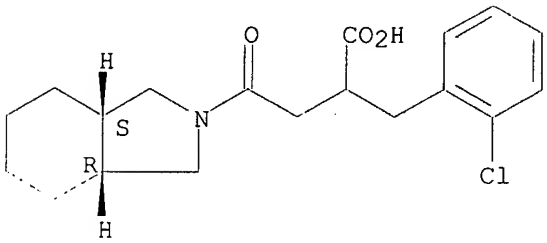
RN 154142-25-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-chlorophenyl)methyl]octahydro-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



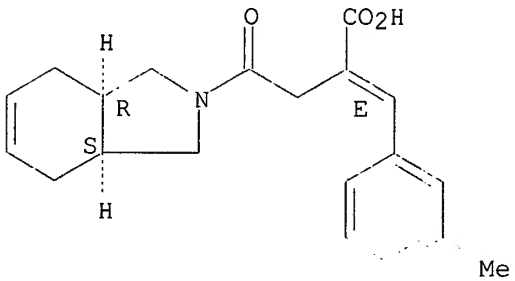
RN 154142-26-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-chlorophenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



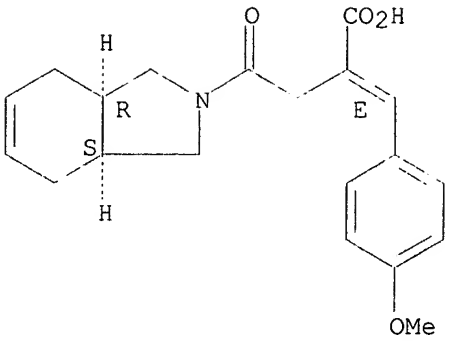
IT **145323-88-2P 145323-89-3P 145323-90-6P**
145323-91-7P 145323-92-8P 145323-96-2P
145323-97-3P 145323-98-4P 145323-99-5P
145324-01-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as intermediate for **antidiabetics**)
RN 145323-88-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(3-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



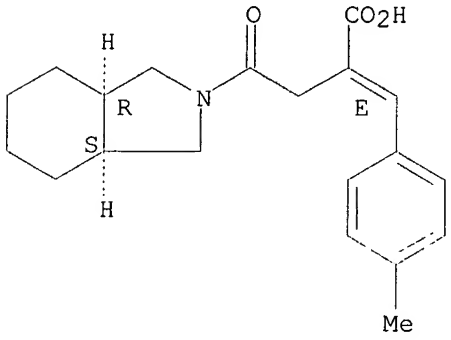
RN 145323-89-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methoxyphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



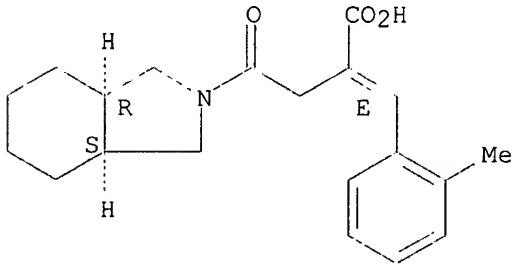
RN 145323-90-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



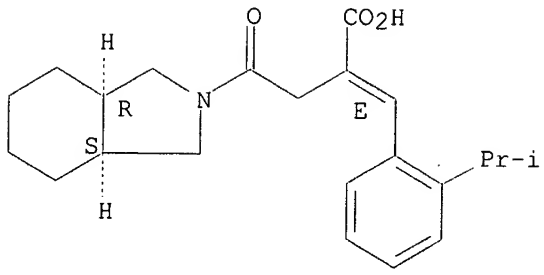
RN 145323-91-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



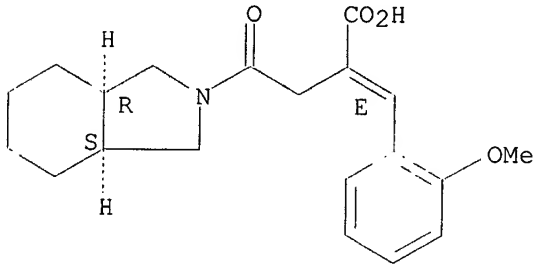
RN 145323-92-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[[2-(1-methylethyl)phenyl]methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



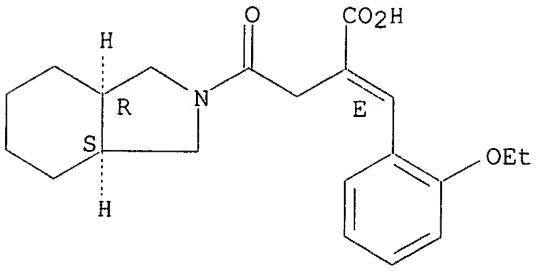
RN 145323-96-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methoxyphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



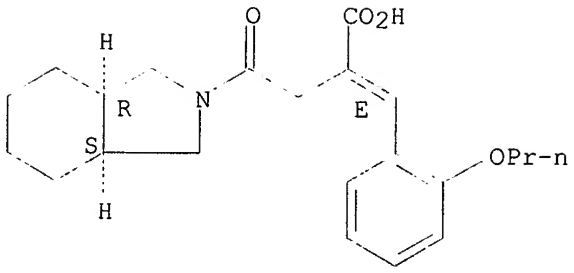
RN 145323-97-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-ethoxyphenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



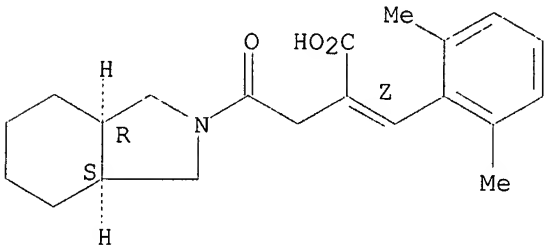
RN 145323-98-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-[(2-propoxyphenyl)methylene]-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



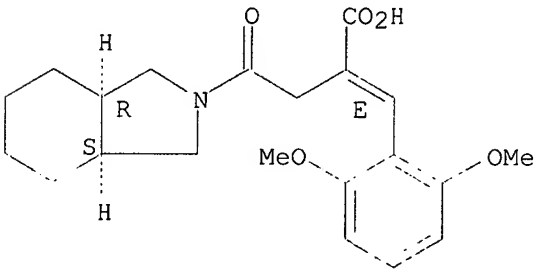
RN 145323-99-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethylphenyl)methylene]octah
ydro-.gamma.-oxo-, [2(Z),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



RN 145324-01-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethoxyphenyl)methylene]octa
hydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L66 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2003 ACS
AN 1993:59584 HCAPLUS
DN 118:59584
TI Preparation of succinic acid azabicyclylamides and related compounds as **antidiabetics**
IN Sato, Fumiyasu; Tsubaki, Atsushi; Hokari, Hiroshi; Tanaka, Nobuyuki; Saito, Masaru; Akahane, Kenji; Kobayashi, Michihiro
PA Kissei Pharmaceutical Co., Ltd., Japan
SO Eur. Pat. Appl., 34 pp.
CODEN: EPXXDW
DT **Patent**
LA English

IC ICM C07D209-08
ICS C07D209-44; C07D217-06; C07D409-06; A61K031-395
CC 27-11 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

	PATENT NO.	KIND	DATE		APPLICATION NO.	DATE	
PI	EP 507534	A1	19921007		EP 1992-302786	19920330	<--
	EP 507534	B1	19960228				
	R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE						
	JP 04330055	A2	19921118		JP 1991-142275	19910330	<--
	JP 04356459	A2	19921210		JP 1991-188416	19910425	<--
	AU 9212809	A1	19921001		AU 1992-12809	19920311	<--
	AU 654331	B2	19941103				
	CA 2062877	AA	19921001		CA 1992-2062877	19920312	<--
	NO 9201200	A	19921001		NO 1992-1200	19920327	<--
	NO 178371	B	19951204				
	NO 178371	C	19960313				
	DK 9200415	A	19921001		DK 1992-415	19920327	<--
	DK 170973	B1	19960409				
	US 5202335	A	19930413		US 1992-860023	19920330	<--
	AT 134615	E	19960315		AT 1992-302786	19920330	<--
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PRAI	JP 1991-142275		19910330	<--			
	JP 1991-188416		19910425	<--			
	JP 1991-361519		19911227	<--			

OS MARPAT 118:59584
AB Title compds. ACHRCR(CO2R1)CH2COB [A = heterocyclyl, C3-8 cycloalkyl, (substituted) Ph; B = bicyclic amino group which may have 1 or 2 unsatd. bonds and is bound to the carbonyl group via the N atom; R = H or RR = bond; R1 = H, C1-6 alkyl, C7-10 aralkyl] were prepd. Thus, cis-hexahydroisoindoline was added to a suspension of (E)-benzylidenesuccinic anhydride and the mixt. was stirred at room temp. for 2 h to give (E)-2-benzylidene-3-(cis-hexahydro-2-isoindolylcarbonyl)propionic acid (I). I reduced blood glucose levels in rats or mice by 44% when force-fed at 3.0 mg/kg.
ST succinic acid azabicyclylamide prepn **antidiabetic**
IT **Antidiabetics** and Hypoglycemics
(succinic acid azabicyclylamides and related compds.)
IT **145323-82-6P 145323-83-7P 145323-84-8P**
145323-85-9P 145323-86-0P 145323-87-1P
145323-88-2P 145323-89-3P 145323-90-6P
145323-91-7P 145323-92-8P 145323-93-9P
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145525-40-2P 145525-41-3P 145525-42-4P 145525-43-5P
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of, as **antidiabetic**)

IT 1141-85-1P 145324-43-2P 145324-44-3P 145324-45-4P 145324-46-5P
145324-47-6P 145324-48-7P 145324-49-8P 145324-50-1P 145324-51-2P
145324-52-3P 145324-53-4P 145324-54-5P 145324-55-6P
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(prepn. of, as intermediate for **antidiabetics**)

IT 67-56-1, Methanol, reactions 71-23-8, Propanol, reactions 83-38-5,
2,6-Dichlorobenzaldehyde 100-39-0, Benzyl bromide 106-65-0, Dimethyl
succinate 106-94-5, Propyl bromide 108-24-7, Acetic anhydride
123-25-1, Diethylsuccinate 334-88-3, Diazomethane 446-52-6,
2-Fluorobenzaldehyde 529-20-4, 2-Methylbenzaldehyde 543-27-1, Isobutyl
chloroformate 613-69-4, 2-Ethoxybenzaldehyde 620-23-5,
3-Methylbenzaldehyde 1123-56-4, 2,6-Dimethylbenzaldehyde 1470-99-1,
cis-Hexahydroisoindoline 2030-29-7, trans-Hexahydroindoline 2043-61-0,
Cyclohexanecarbaldehyde 2144-87-8 2395-99-5, 4-Nitrophenyl
2744-09-4, trans-Decahydroisoquinoline 3392-97-0, 2,6-
Dimethoxybenzaldehyde 6502-22-3, 2-Isopropylbenzaldehyde 7091-12-5,
2-Propoxybenzaldehyde 10479-63-7, trans-Hexahydroisoindoline
15822-93-2 33446-22-9 46427-07-0 116129-80-7 140903-48-6
142210-40-0 145324-56-7 145324-57-8 145324-58-9 145324-59-0
145324-60-3 145324-61-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in prepn. of **antidiabetics**)

IT **145323-82-6P 145323-83-7P 145323-84-8P**
145323-85-9P 145323-86-0P 145323-87-1P
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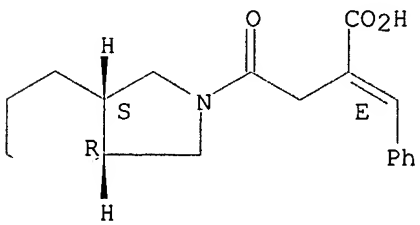
145324-40-9P 145324-41-0P 145324-42-1P
145375-43-5P 145375-44-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as **antidiabetic**)

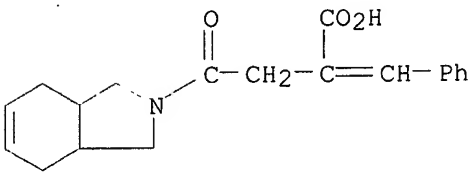
RN 145323-82-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-
(phenylmethylene)-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

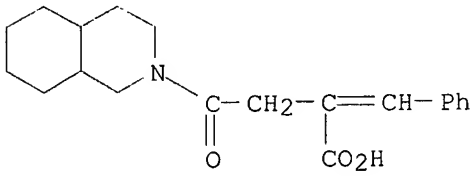


RN 145323-83-7 HCAPLUS

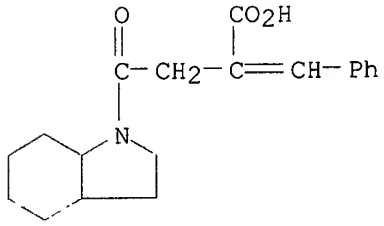
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



RN 145323-84-8 HCAPLUS
CN 2(1H)-Isoquinolinebutanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, [2(E),4a.alpha.,8a.beta.]- (9CI) (CA INDEX NAME)

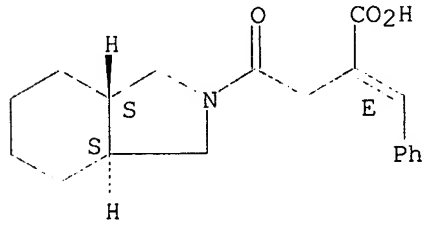


RN 145323-85-9 HCAPLUS
CN 1H-Indole-1-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)- (9CI) (CA INDEX NAME)

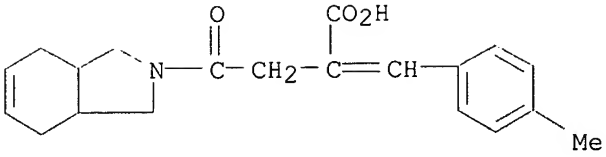


RN 145323-86-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, [2(E),3a.alpha.,7a.beta.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

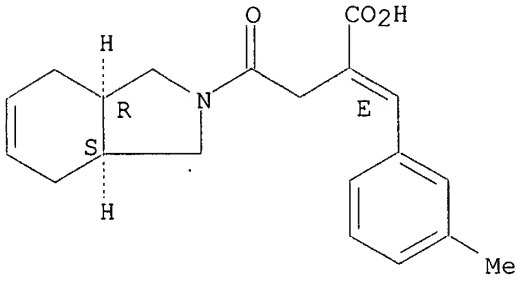


RN 145323-87-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



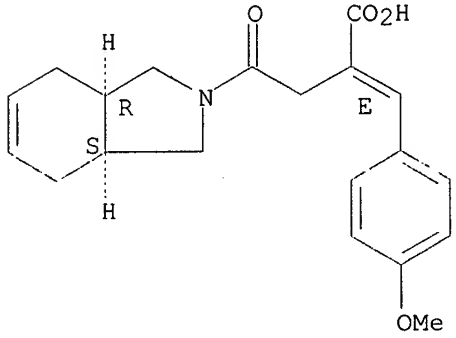
RN 145323-88-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(3-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



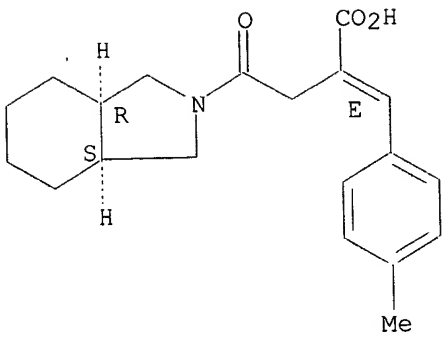
RN 145323-89-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methoxyphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



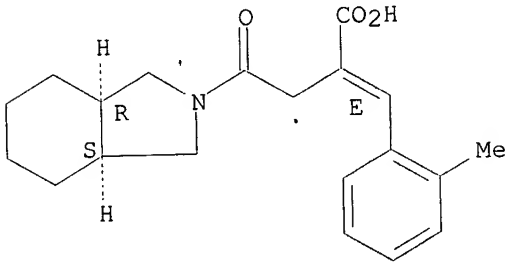
RN 145323-90-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



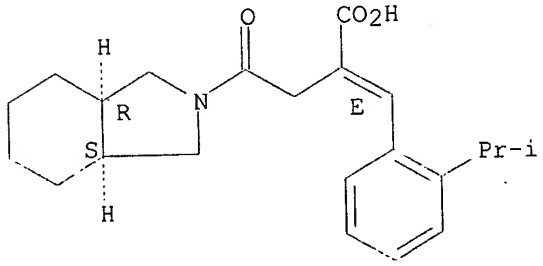
RN 145323-91-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

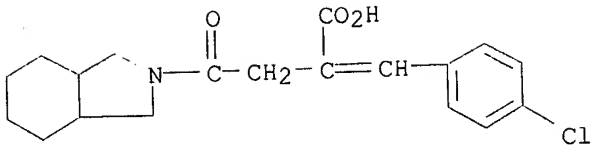


RN 145323-92-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[[2-(1-methylethyl)phenyl]methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

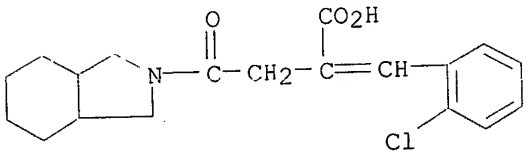
Relative stereochemistry.
Double bond geometry as shown.



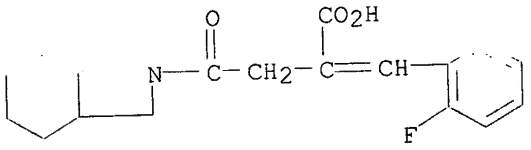
RN 145323-93-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(4-chlorophenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



RN 145323-94-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-chlorophenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

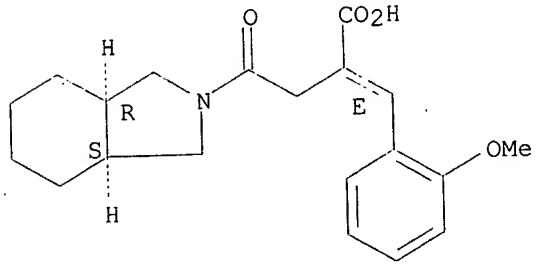


RN 145323-95-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-fluorophenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



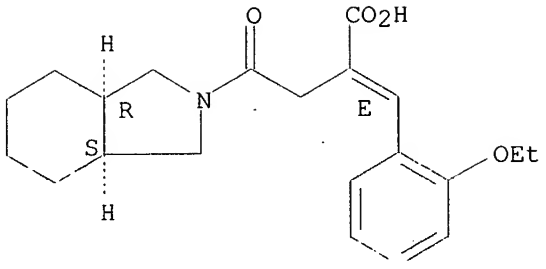
RN 145323-96-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methoxyphenyl)methylene]-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



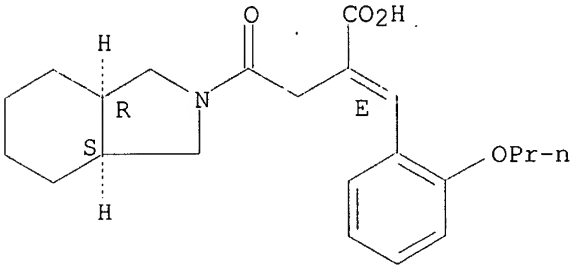
RN 145323-97-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-ethoxyphenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



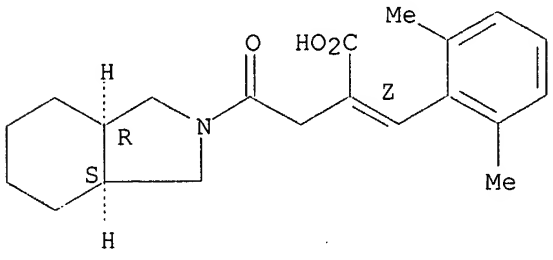
RN 145323-98-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-[(2-propoxyphenyl)methylene]-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

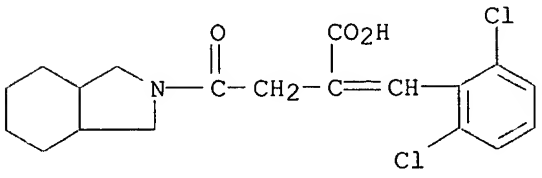


RN 145323-99-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethylphenyl)methylene]octahydro-.gamma.-oxo-, [2(Z),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

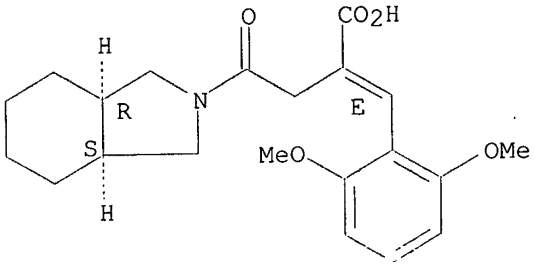


RN 145324-00-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dichlorophenyl)methylene]octahydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



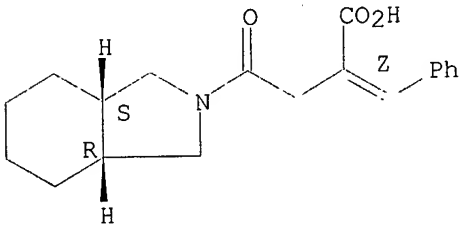
RN 145324-01-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethoxyphenyl)methylene]octa hydro-.gamma.-oxo-, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



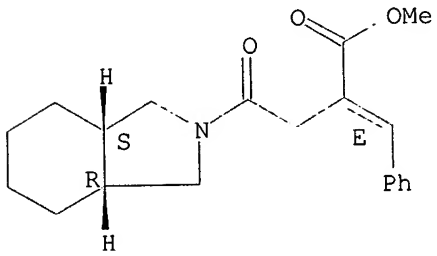
RN 145324-04-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, [2(Z),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

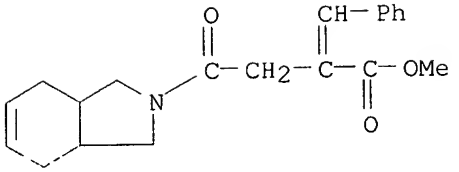


RN 145324-05-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

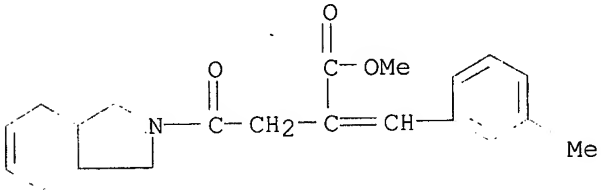
Relative stereochemistry.
Double bond geometry as shown.



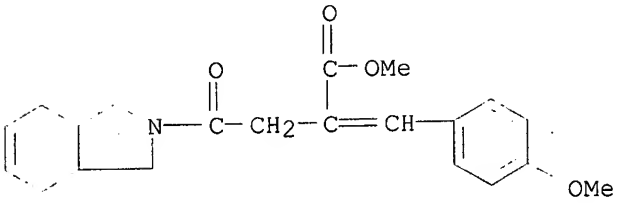
RN 145324-06-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



RN 145324-07-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(3-methylphenyl)methylene]-.gamma.-oxo-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

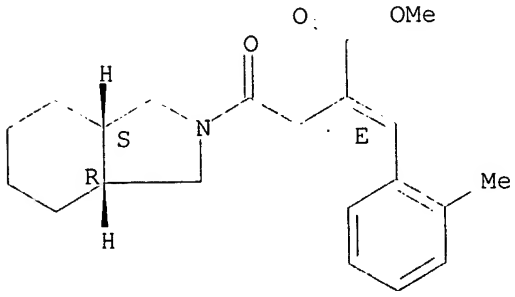


RN 145324-08-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methoxyphenyl)methylene]-.gamma.-oxo-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



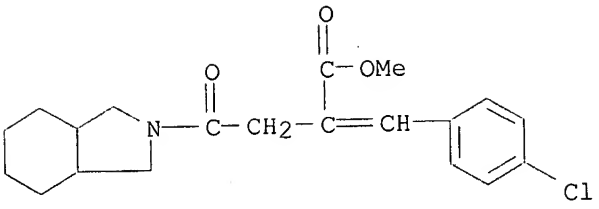
RN 145324-09-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methylene]-.gamma.-oxo-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.

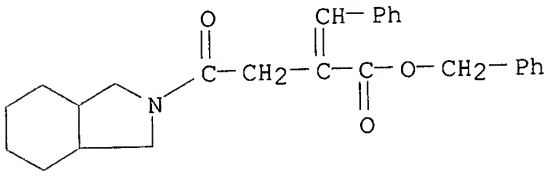


RN 145324-10-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(4-chlorophenyl)methylene]octahydro-.gamma.-oxo-, methyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX

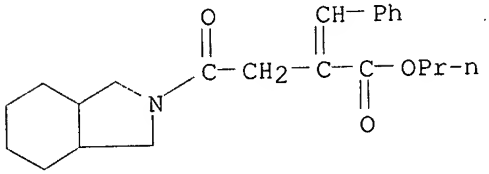
NAME)



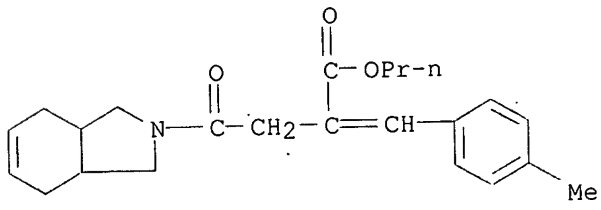
RN 145324-11-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, phenylmethyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



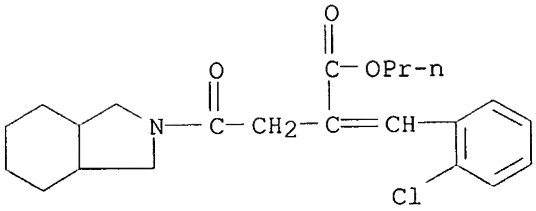
RN 145324-12-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, propyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



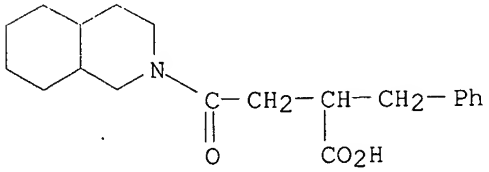
RN 145324-13-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methylphenyl)methylene]-.gamma.-oxo-, propyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



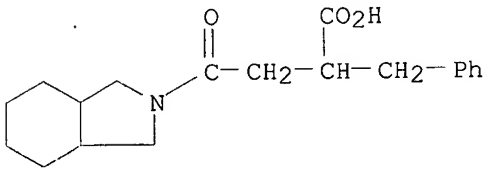
RN 145324-14-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-chlorophenyl)methylene]octahydro-.gamma.-oxo-, propyl ester, [2(E),3a.alpha.,7a.alpha.]- (9CI) (CA INDEX NAME)



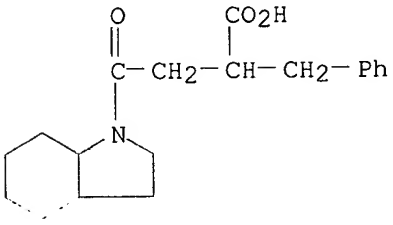
RN 145324-15-8 HCAPLUS
CN 2(1H)-Isoquinolinebutanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 145324-16-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)

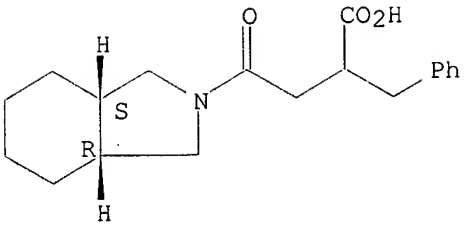


RN 145324-17-0 HCAPLUS
CN 1H-Indole-1-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)- (9CI) (CA INDEX NAME)



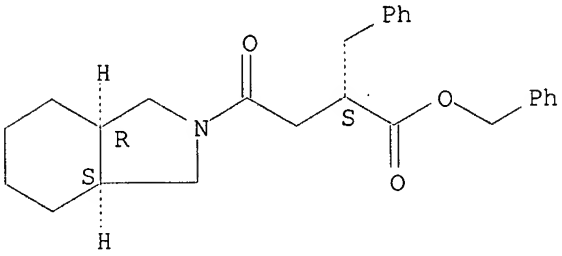
RN 145324-18-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



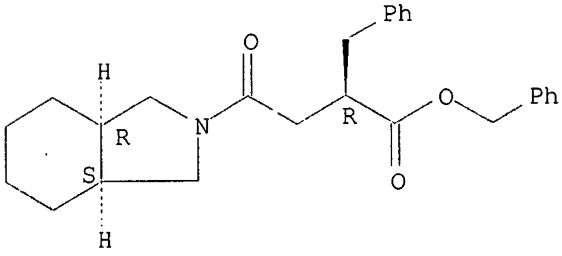
RN 145324-19-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, phenylmethyl ester, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



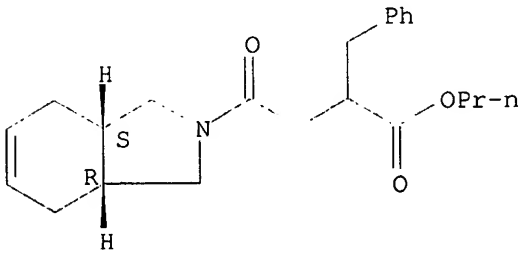
RN 145324-20-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, phenylmethyl ester, [2(R)-cis]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 145324-21-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, propyl ester, cis- (9CI) (CA INDEX NAME)

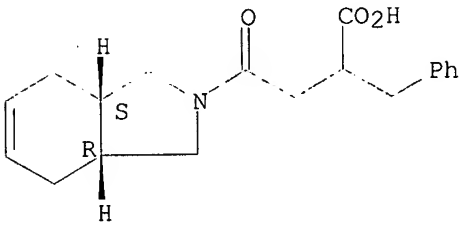
Relative stereochemistry.



RN 145324-22-7 HCAPLUS

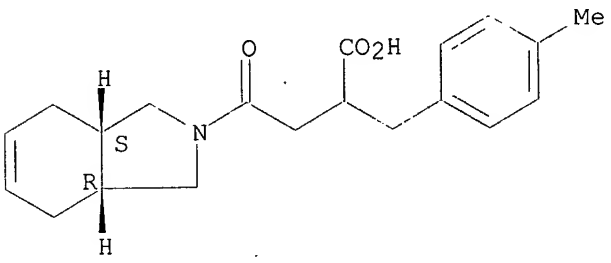
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



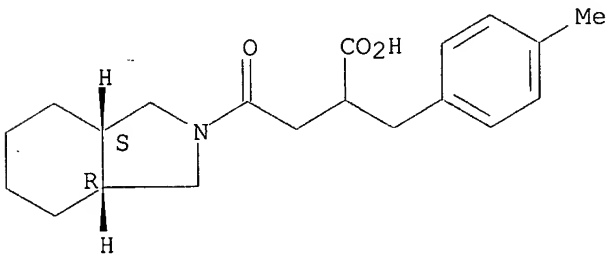
RN 145324-23-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, 1,3,3a,4,7,7a-hexahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



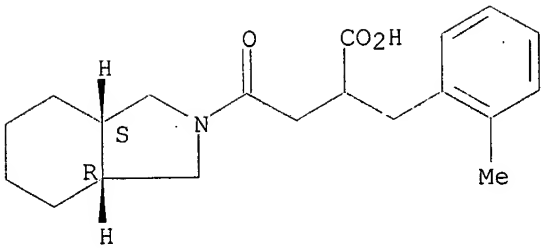
RN 145324-24-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



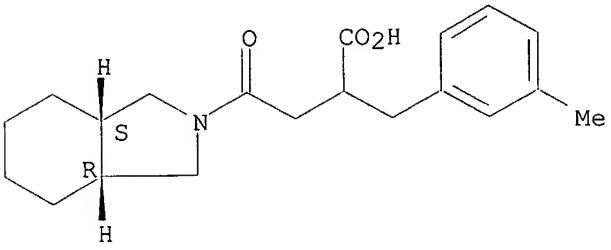
RN 145324-25-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



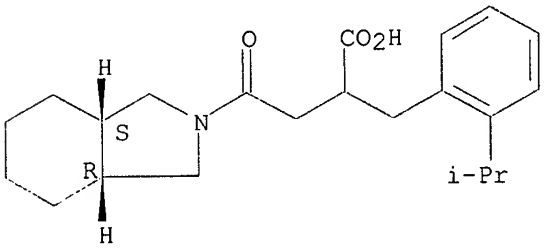
RN 145324-26-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(3-methylphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



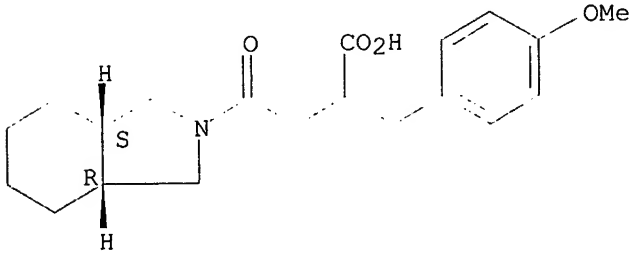
RN 145324-27-2 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[[2-(1-methylethyl)phenyl]methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



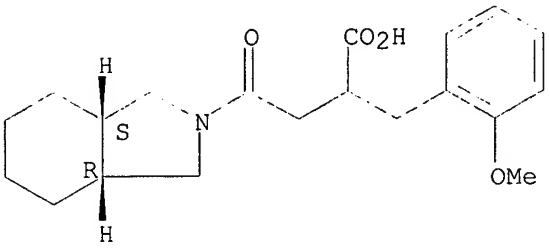
RN 145324-28-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methoxyphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



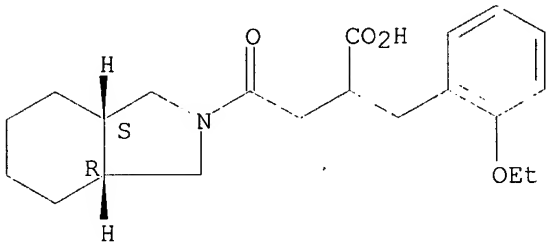
RN 145324-29-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methoxyphenyl)methyl]-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



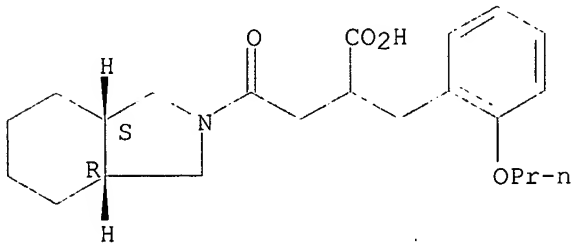
RN 145324-30-7 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2-ethoxyphenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



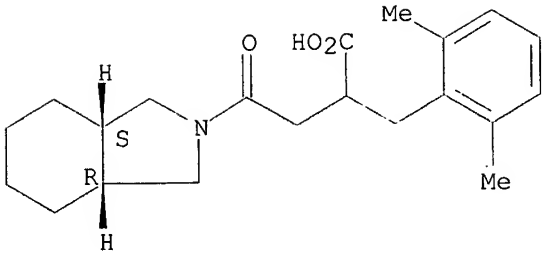
RN 145324-31-8 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-[(2-propoxyphenyl)methyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



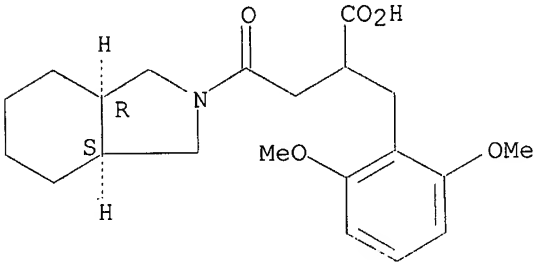
RN 145324-32-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethylphenyl)methyl]octahydro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



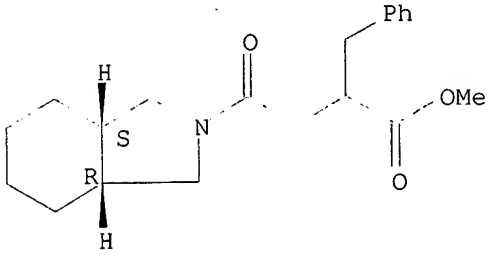
RN 145324-33-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, .alpha.-[(2,6-dimethoxyphenyl)methyl]octahyd
ro-.gamma.-oxo-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



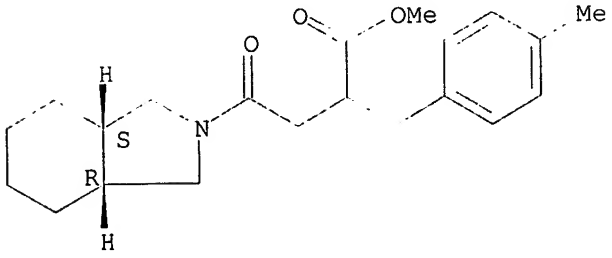
RN 145324-36-3 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-
, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



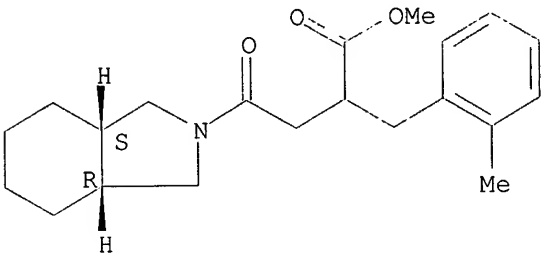
RN 145324-37-4 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-
.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



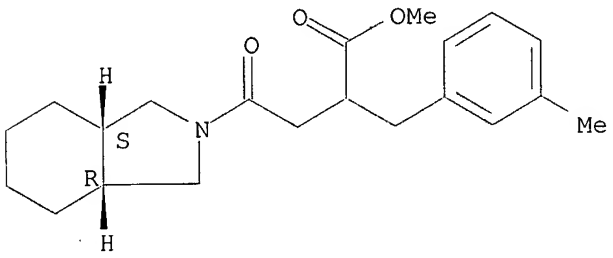
RN 145324-38-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(2-methylphenyl)methyl]-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



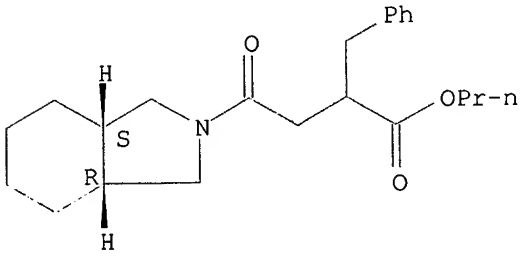
RN 145324-39-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(3-methylphenyl)methyl]-.gamma.-oxo-, methyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



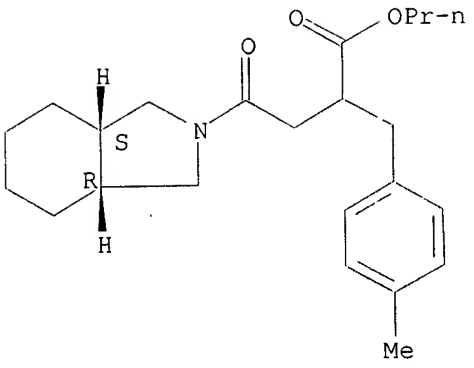
RN 145324-40-9 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, propyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



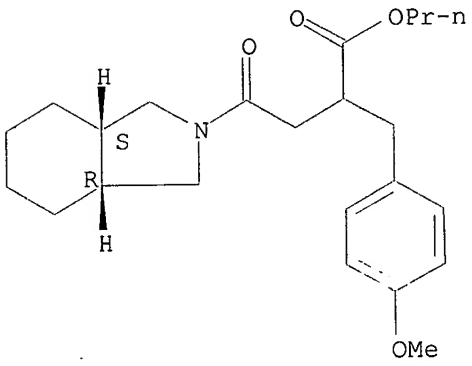
RN 145324-41-0 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methylphenyl)methyl]-.gamma.-oxo-, propyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



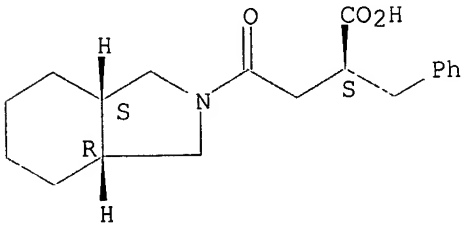
RN 145324-42-1 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.alpha.-[(4-methoxyphenyl)methyl]-.gamma.-oxo-, propyl ester, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



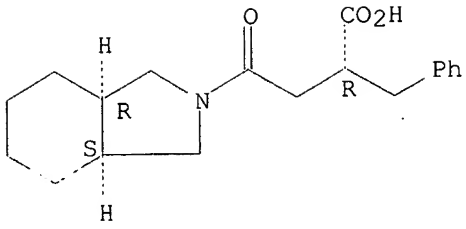
RN 145375-43-5 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 145375-44-6 HCAPLUS
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.R,3aR,7aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> fil reg
FILE 'REGISTRY' ENTERED AT 17:42:50 ON 04 MAR 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 3 MAR 2003 HIGHEST RN 496834-05-0
DICTIONARY FILE UPDATES: 3 MAR 2003 HIGHEST RN 496834-05-0

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

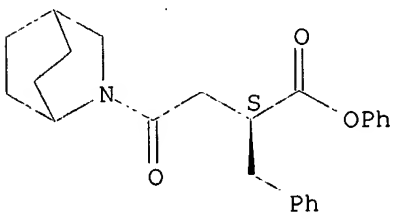
Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> d ide can tot

L78 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-88-9 REGISTRY
CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, phenyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H27 N O3**
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



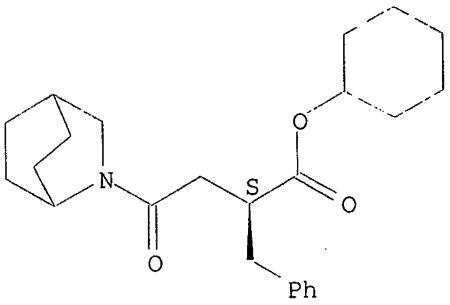
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-87-8 REGISTRY
CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, cyclohexyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C24 H33 N O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



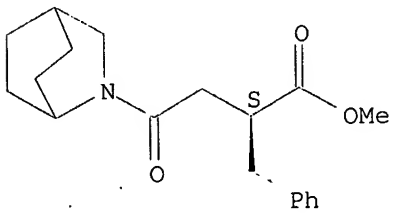
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-86-7 REGISTRY
CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, methyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C19 H25 N O3**
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



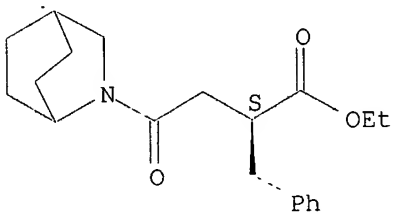
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-85-6 REGISTRY
CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, ethyl ester, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C20 H27 N O3**
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



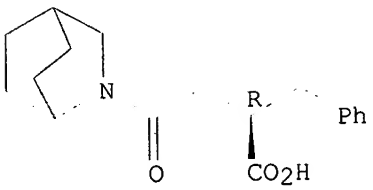
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-80-1 REGISTRY
CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H23 N O3**
CI COM
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

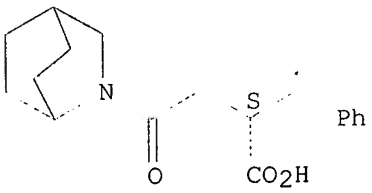
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 465526-73-2 REGISTRY

CN 2-Azabicyclo[2.2.2]octane-2-butanoic acid, .gamma.-oxo-.alpha.-(phenylmethyl)-, (.alpha.S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H23 N O3**
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT

Absolute stereochemistry.



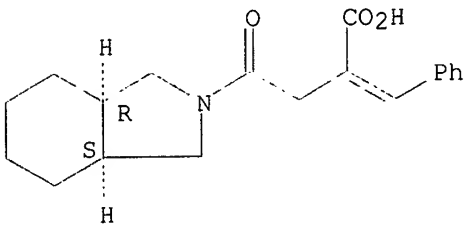
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 137:279359

L78 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 219712-08-0 REGISTRY
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethylene)-, (3aR,7aS)-rel- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C19 H23 N O3**
SR CA
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Relative stereochemistry.
Double bond geometry unknown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

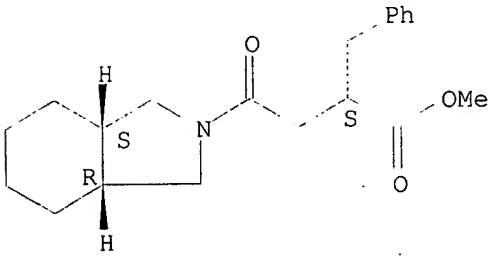
1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 130:110156

L78 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2003 ACS
RN 204187-39-3 REGISTRY
CN 2H-Isoindole-2-butanoic acid, octahydro-.gamma.-oxo-.alpha.-(phenylmethyl)-, methyl ester, [2(S)-[2(R*),3a.alpha.,7a.alpha.]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C20 H27 N O3**

SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1962 TO DATE)
1 REFERENCES IN FILE CAPLUS (1962 TO DATE)

REFERENCE 1: 128:217248

=> d his

(FILE 'HOME' ENTERED AT 17:07:25 ON 04 MAR 2003)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 17:07:38 ON 04 MAR 2003

L1		STR
L2	42	S L1
L3		STR L1
L4	10	S L3
L5	721	S L2 FUL
		SAV L5 KWON030/A
L6	423	S L3 FUL SUB=L5
		SAV L6 KWON030A/A
L7		STR L3
L8	5	S L7 CSS SAM SUB=L6
L9		STR L7
L10	5	S L9 CSS SAM SUB=L6
L11	164	S L9 CSS FUL SUB=L6
		SAV L11 KWON030B/A
L12	133	S L11 AND 1/NC
L13	15	S L12 AND (NC4-C6-C6 OR NC4-OC4 OR NC4-SC4)/ES
L14	10	S L12 AND (OXIREN? OR DIOX? OR EPOX?)
L15	108	S L12 NOT L13,L14
L16	9	S L15 AND METHANO?
L17	99	S L15 NOT L16
L18	21	S L17 AND SPIRO
L19	78	S L17 NOT L18

FILE 'HCAPLUS' ENTERED AT 17:23:39 ON 04 MAR 2003

L20	34	S L19
L21	1	S L18
L22	35	S L20,L21
		E CAILLE D/AU
L23	21	S E3,E5
L24	3679	S (SANOFI? OR SYNTHELABO?)/PA,CS
L25	2	S L22 AND L23,L24

```
L26      187625 S ?ARTHRIT? OR ?INFLAM?
                E ARTHRITIS/CT
L27       11734 S E3-E25
                E E3+ALL
L28       20616 S E6+NT
                E E19+ALL
L29        4559 S E5,E4+NT
                E INFLAMMATION/CT
L30       48599 S E3-E24
                E E3+ALL
L31       75108 S E2+NT
L32       15998 S E35+NT OR E37+NT OR E38+NT
                E E36+ALL
L33       48702 S  E4,E5,E3+NT
L34           2 S L22 AND L26-L33
L35           3 S L25,L34
L36          28 S L22 AND (?DIABET? OR ?RETINOPATH?)
L37           3 S L22 AND (?DIABET? AND ?RETINOPATH?)
                E RETINOPATHY/CT
                E E3+ALL
L38        2626 S E2
                E DIABETIC RETINOPATHY/CT
                E E3+ALL
L39        1524 S E2
L40           2 S L22 AND L38,L39
L41           5 S L35,L37,L40
                E LUMBAGO/CT
L42           0 S L22 AND LUMBAGO
L43           0 S L22 AND PAIN?
L44           0 S L22 AND ?TRAUMA?
L45           2 S L22 AND ANALGES?
                E ANTIPYRETIC/CT
L46           1 S L22 AND E8,E9
                E 8+ALL
                E ANTIPYRETIC/CT
                E E8+ALL
L47           1 S L22 AND E3+NT
                E E11+ALL
L48           0 S L22 AND E3,E2+NT
L49           0 S L22 AND (FEVER? OR HYPERTHERM? OR HYPERPYREX? OR PYREX?)
L50           5 S L41,L45,L46,L47
L51          18 S (L19 OR L18)(L)THU/RL
L52          13 S L51 NOT L50
L53           2 S L22 AND (ENT OR EYE OR NOSE OR ?NASAL? OR THROAT)
L54           5 S L50,L53
L55          28 S L22 AND P/DT
L56          23 S L22 AND (PD<=20000509 OR PRD<=20000509 OR AD<=20000509)
L57           2 S L56 AND L54
L58          19 S L56 AND L55
L59           3 S L54 NOT L57
L60          17 S L58 AND L26-L54
                SEL DN AN 1-3
L61          14 S L60 NOT E1-E9
L62           6 S L56 NOT L57,L60
L63           1 S L62 AND (1 OR 63)/SC,SX
L64           2 S L62 AND ?DIABET?
L65          16 S L57,L61,L63,L64
L66          16 S L25,L65
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 17:37:31 ON 04 MAR 2003
L67          91 S E10-E100
L68           1 S 145375-43-5
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L69          25 S C19H25NO3 AND L5
L70          10 S L69 AND 1/NC
L71           6 S L70 AND L6
L72           4 S L71 AND  ISOINDOL?

     FILE 'HCAPLUS' ENTERED AT 17:39:54 ON 04 MAR 2003
L73          27 S L68 OR L72
L74          16 S L73 AND L56
L75          12 S L74 AND P/DT
L76           1 S L74 AND L26-L33,L38-L39,L45-L47

     FILE 'REGISTRY' ENTERED AT 17:40:52 ON 04 MAR 2003

     FILE 'HCAPLUS' ENTERED AT 17:41:22 ON 04 MAR 2003
               SEL HIT RN L66

     FILE 'REGISTRY' ENTERED AT 17:42:27 ON 04 MAR 2003
L77          91 S E101-E191
L78           8 S L17,L18,L19 NOT L77

     FILE 'REGISTRY' ENTERED AT 17:42:50 ON 04 MAR 2003
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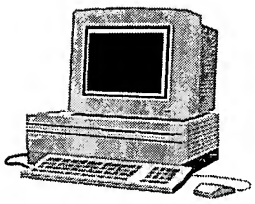
BioTech-Chem Library
Search Results
Feedback Form (Optional)



Scientific & Technical Information Center

The search results generated for your recent request are attached. If you have any questions or comments (compliments or complaints) about the scope or the results of the search, please contact ***the BioTech-Chem searcher*** who conducted the search ***or contact***:

Mary Hale, Supervisor, 308-4258
CM-1 Room 1E01

Voluntary Results Feedback Form

- *I am an examiner in Workgroup:* *(Example: 1610)*
- *Relevant prior art **found**, search results used as follows:*
  - ☐ 102 rejection
  - ☐ 103 rejection
  - ☐ Cited as being of interest.
  - ☐ Helped examiner better understand the invention.
  - ☐ Helped examiner better understand the state of the art in their technology.

  Types of relevant prior art found:
  - ☐ Foreign Patent(s)
  - ☐ Non-Patent Literature
    (journal articles, conference proceedings, new product announcements etc.)
- *Relevant prior art **not found**:*
  - ☐ Results verified the lack of relevant prior art (helped determine patentability).
  - ☐ Search results were not useful in determining patentability or understanding the invention.

Other Comments:

Drop off completed forms at the **Circulation Desk CM-1,** or send to Mary Hale, **CM1-1E01 or e-mail mary.hale@uspto.gov.**